

SEARCH REQUEST FORM

Requestor's

Name: PAUL J. SAMP

Serial

Number: 00101 05

Date: 12/4/78

Phone: 8-4221

Art Unit: 1048

Search Topic:

Please write a detailed statement of search topic. Describe specifically as possible the subject matter to be searched. Define any terms that may have a special meaning. Give examples or relevant citations, authors, keywords, etc., if known. For sequences, please attach a copy of the sequence. You may include a copy of the broadest and/or most relevant claim(s).

Please search the attached chemical structure. Particular emphasis should be placed on the compounds MURAMETIDE & MURAMETIDE (see names 18 & 19).

② I am also interested in knowing if immunophorin has been used in the treatment of viral infections (i.e., RNA viruses, DNA viruses, retroviruses, etc.), particularly in relation to HIV-1, HIV-2, & HIV Human and simian immunodeficiency viruses).

T. L. L.

STAFF USE ONLY

Date completed: _____

Searcher: _____

Terminal time: _____

Elapsed time: _____

CPU time: _____

Total time: _____

Number of Searches: _____

Number of Databases: _____

Search Site

_____ STIC

_____ CM-1

_____ Pre-S

Type of Search

_____ N.A. Sequence

_____ A.A. Sequence

_____ Structure

_____ Bibliographic

Vendors

_____ IG

_____ STN

_____ Dialog

_____ APS

_____ Geninfo

_____ SDC

_____ DARC/Questel

_____ Other

TI Synthetic peptides, compositions containing them, and their use for diagnosis and vaccination for **AIDS** and ARC.
 IN Kennedy, Ronald C.; Dreesman, Gordon R.; Essex, Myron
 PA Southwest Foundation for Biomedical Research, USA; Harvard College
 SO PCT Int. Appl., 41 pp.
 CODEN: PIXXD2

DT **Patent**

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 8702775	A1	19870507	WO 86-US2234	19861022
	W: JP				
	RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
	EP 245362	A1	19871119	EP 86-906660	19861022
	EP 245362	B1	19940629		
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	JP 63501716	T2	19880714	JP 86-505826	19861022
	US 4956273	A	19900911	US 89-331052	19890328
PRAI	US 85-790830		19851024		
	WO 86-US2234		19861022		
	US 88-203609		19880602		

AB Synthetic peptides homologous to the gp 41 and gp 120 subunits of the gp 160 envelope glycoprotein of human T-cell lymphotropic virus type III (HTLV-III) are prepd. for use in detection of antibodies to and vaccination against the viral causative agents of **AIDS** and ARC (**AIDS**-related complex). Hydrophilic regions and regions with .beta.-turns were identified by computer anal. on gp 120, gp 41, and gp 160 as potential immunogenic sites and used as a basis for synthesis of peptides by the Merrifield method. A peptide corresponding to residues 735-752 of gp 120 was conjugated to keyhole limpet hemocyanin for induction of antibody in rabbits. In an assay for diagnosis of **AIDS** by serum antibody detection, an insol. support matrix was coated with a conjugate of this peptide with albumin, incubated with a serum sample, washed, incubated with biotin-labeled goat anti-human Ig followed by an avidin-peroxidase conjugate, H2O2, and a chromogenic substrate.

IT **53678-77-6D**, Muramyl dipeptide, conjugates

74817-61-1D, conjugates

RL: BIOL (Biological study)

(with peptides homologous to **AIDS** virus envelope glycoproteins)

L62 ANSWER 23 OF 23 HCAPLUS COPYRIGHT 1998 ACS

AN 1987:475611 HCAPLUS

DN 107:75611

TI Method and test-kit to detect and/or monitor a pathological condition

IN Spillert, Charles R.; Suval, William A.; Lazaro, Eric J.

PA University of Medicine and Dentistry of New Jersey, USA

SO PCT Int. Appl., 37 pp.

CODEN: PIXXD2

DT **Patent**

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 8606840	A1	19861120	WO 86-US1075	19860516
	W: AU, BR, DK, JP, NO, US				

=> fil reg

FILE 'REGISTRY' ENTERED AT 09:06:53 ON 08 DEC 1998
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 PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
 COPYRIGHT (C) 1998 American Chemical Society (ACS)

STRUCTURE FILE UPDATES: 6 DEC 98 HIGHEST RN 215160-44-4
 DICTIONARY FILE UPDATES: 7 DEC 98 HIGHEST RN 215160-44-4

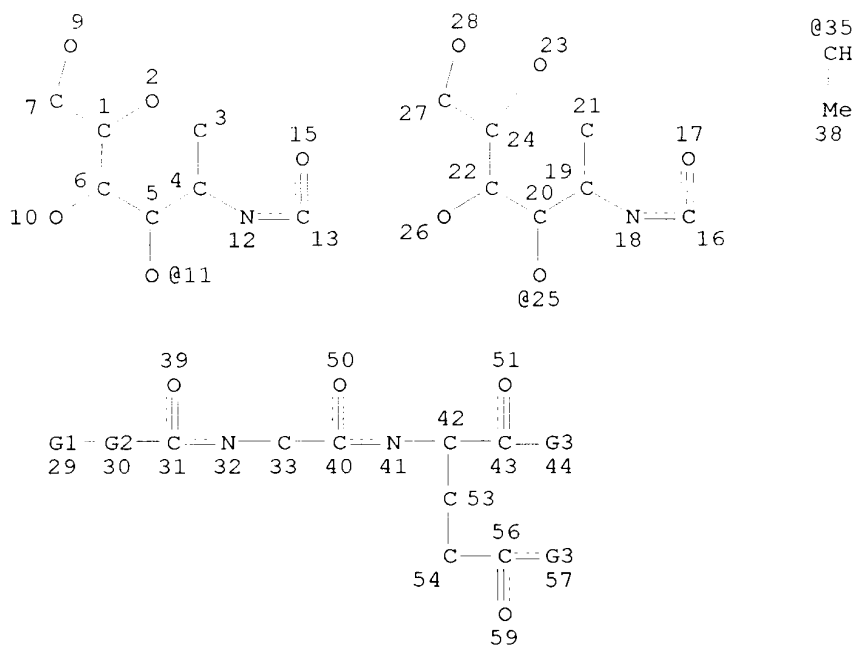
TSCA INFORMATION NOW CURRENT THROUGH JUNE 29, 1998

Please note that search-term pricing does apply when
 conducting SmartSELECT searches.

=> d stat que 132

L18

STR



VAR G1=11/25

VAR G2=CH2/35

VAR G3=O/N

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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

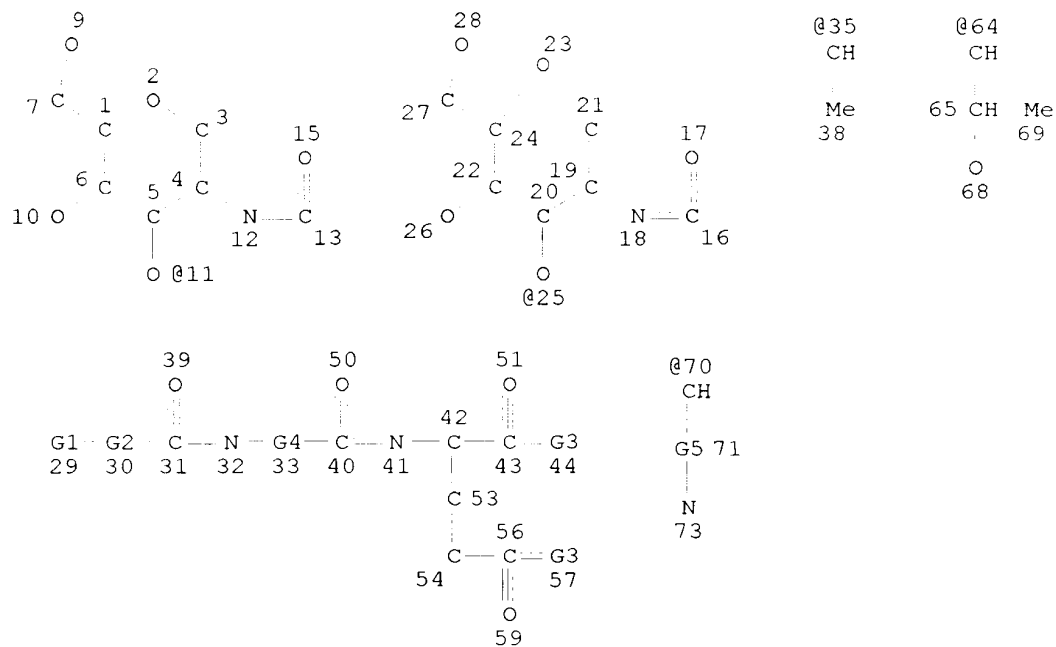
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NUMBER OF NODES IS 46

STEREO ATTRIBUTES: NONE

L20

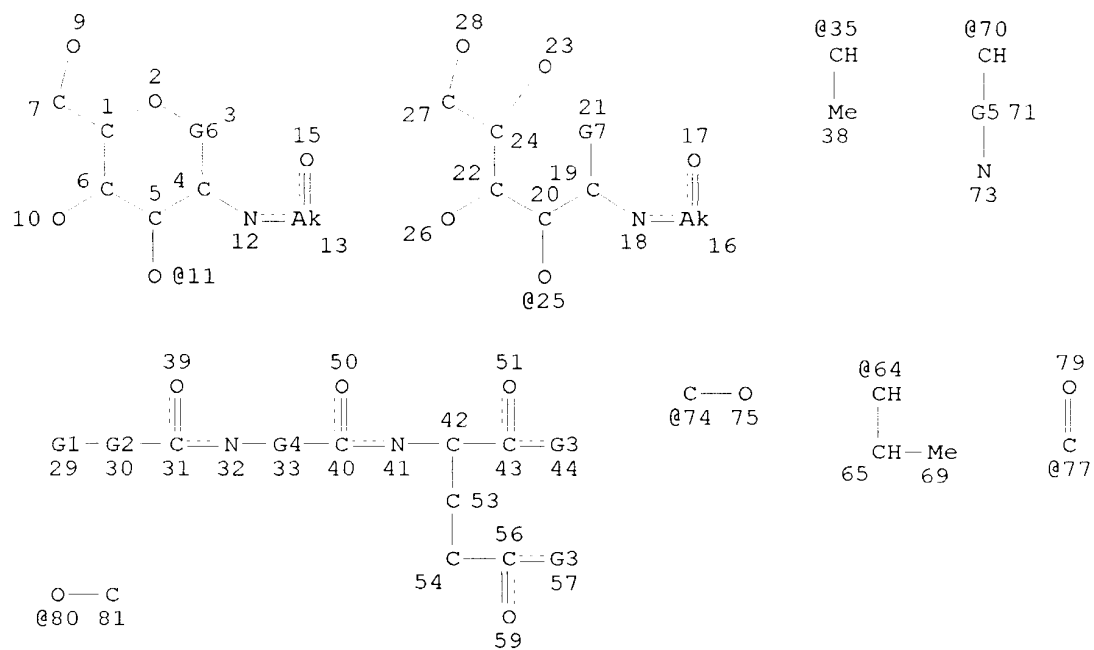
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VAR G1=11/25
 VAR G2=CH2/35
 VAR G3=O/N
 VAR G4=35/64/70
 REP G5=(4-4) CH2
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 DEFAULT MLEVEL IS ATOM
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
 RING(S) ARE ISOLATED OR EMBEDDED
 NUMBER OF NODES IS 53

STEREO ATTRIBUTES: NONE
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 L24 2373 SEA FILE=REGISTRY SUB=L23 SSS FUL L20
 L27 STR



VAR G1=11/25
 VAR G2=CH2/35
 VAR G3=O/N/80
 VAR G4=35/64/70
 REP G5=(4-4) CH2
 VAR G6=C/74
 VAR G7=C/77

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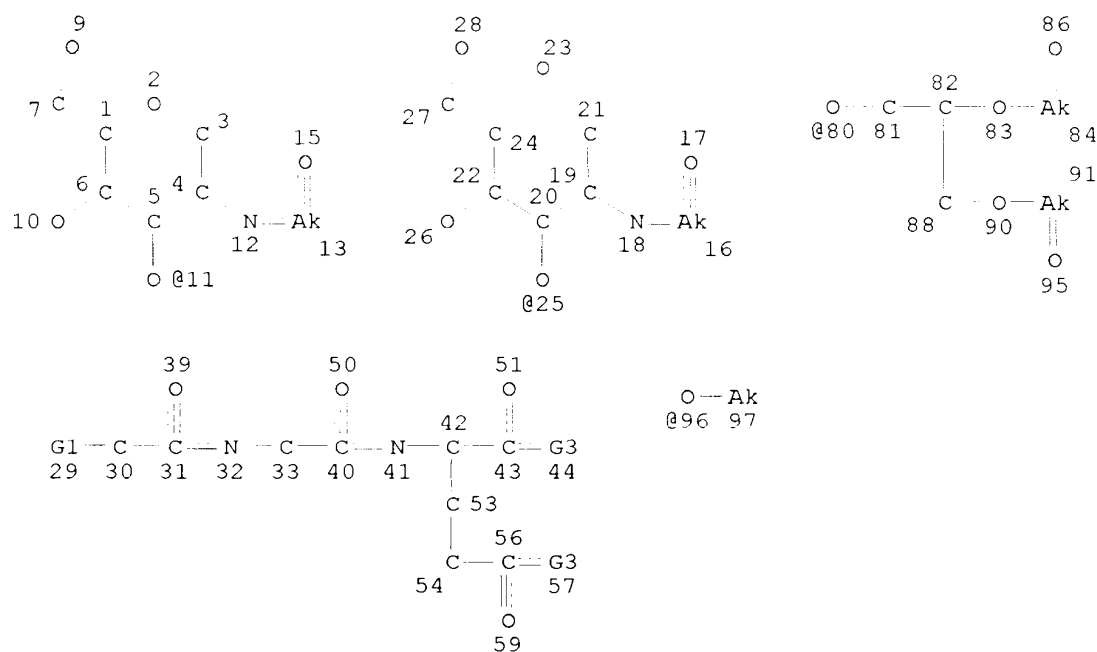
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 DEFAULT ECLEVEL IS LIMITED
 ECOUNT IS E2 C AT 13
 ECOUNT IS E2 C AT 16

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STEREO ATTRIBUTES: NONE

L29 130 SEA FILE=REGISTRY SUB=L24 CSS FUL L27
 L30 STR



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VAR G3=O/N/96/80

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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 56

STEREO ATTRIBUTES: NONE

L32 111 SEA FILE=REGISTRY SUB=L29 CSS FUL L30

100.0% PROCESSED 130 ITERATIONS
SEARCH TIME: 00.00.01

111 ANSWERS

=> d his 13-14

(FILE 'HCAPLUS' ENTERED AT 08:20:51 ON 08 DEC 1998)

E BAHR G/AU
L3 68 S E3-E10
E VACSYN/PA,CS
L4 18 S E3-E15

=> d his 133-

(FILE 'REGISTRY' ENTERED AT 08:23:57 ON 08 DEC 1998)
SAV L32 PARKIN809C/A

FILE 'HCAPLUS' ENTERED AT 08:57:12 ON 08 DEC 1998
L33 1350 S L32
L34 37 S L3, L4 AND L33
L35 15 S L33 AND HIV
L36 11 S L33 AND AIDS
L37 4 S L33 AND ACQUIR?(L) IMMUNODEFICIEN?
L38 25 S L33 AND HUMAN(L) IMMUNODEFICIEN?
L39 24 S L38 AND VIRUS?/CW (L) IMMUNODEFICIEN?
L40 24 S L38 AND L39
L41 30 S L35-L40
L42 6 S L34 AND L41

FILE 'REGISTRY' ENTERED AT 09:01:03 ON 08 DEC 1998
E MURAMETIDE/CN
L43 1 S E3
E MURABUTIDE/CN
L44 1 S E3
E GM-CSF/CN
L45 1 S E3
E PROTEASE/CN
L46 1 S E3
E RETROPEP/CN
L47 1 S E4

FILE 'HCAPLUS' ENTERED AT 09:01:59 ON 08 DEC 1998
L48 105982 S L45 OR L46 OR L47 OR GMCSF OR GM CSF OR COLONY (L) STIM
L49 46 S L48 AND L33
L50 5 S L49 AND L41
L51 128 S L33 AND INTERFERON
L52 7 S L51 AND L41
L53 267 S L33 AND (CYTOKIN? OR LYMPHOKIN?)
L54 6 S L53 AND L41
L55 2 S L33 AND KAPOSI?
L56 119 S L43 OR L44 OR MURAMETIDE OR MURABUTIDE
L57 4 S L56 AND L41
L58 16 S L56 AND L3, L4
L59 3 S L58 AND L41
L60 15 S L42, L50, L52, L54, L55, L57, L59
L61 21 S L41 AND P/DT
L62 23 S L61, L60
SEL HIT RN

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L63 24 S E1-E24

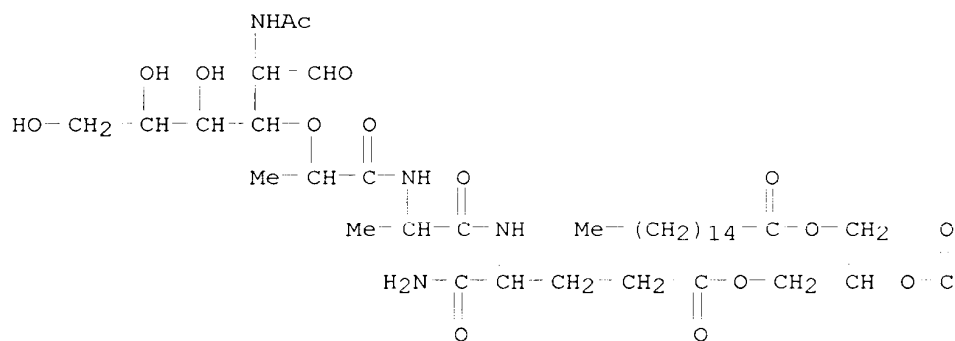
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=> d ide can tot 163

handwritten:
= hit comp'd from
up 1-33, 204
L63

L63 ANSWER 1 OF 24 REGISTRY COPYRIGHT 1998 ACS
RN 127179-83-3 REGISTRY
CN D-.alpha.-Glutamine, N2-[N-(N-acetylmuramoyl)-L-alanyl]-,
2,3-bis[(1-oxohexadecyl)oxy]propyl ester, (R)- (9CI) (CA INDEX

NAME)
 DR 159593-41-6, 159652-90-1
 MF C54 H98 N4 O15
 SR CA
 LC STN Files: CA, CAPLUS, TOXLIT

PAGE 1-A



PAGE 1-B

— (CH₂)₁₄—Me

4 REFERENCES IN FILE CA (1967 TO DATE)
 4 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 122:23868
 REFERENCE 2: 117:118496
 REFERENCE 3: 113:70893
 REFERENCE 4: 112:233710

L63 ANSWER 2 OF 24 REGISTRY COPYRIGHT 1998 ACS

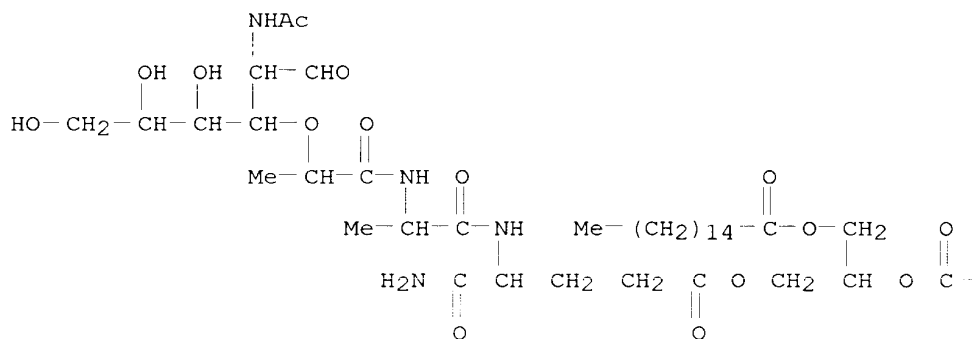
RN **127088-99-7** REGISTRY

CN D-.alpha.-Glutamine, N2-[N-(N-acetylmuramoyl)-D-alanyl]-,
 2,3-bis[(1-oxohexadecyl)oxy]propyl ester, (R)- (9CI) (CA INDEX
 NAME)

DR 155612-56-9

MF C54 H98 N4 O15
 SR CA
 LC STN Files: CA, CAPLUS

PAGE 1-A



PAGE 1-B

— (CH₂)₁₄—Me

4 REFERENCES IN FILE CA (1967 TO DATE)
 4 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 122:23868
 REFERENCE 2: 121:7303
 REFERENCE 3: 120:215331
 REFERENCE 4: 112:233710

L63 ANSWER 3 OF 24 REGISTRY COPYRIGHT 1998 ACS
 RN **125637-74-3** REGISTRY
 CN D-Glutamic acid, N-[N-(N-acetylisomuramoyl)-L-alanyl]-, dimethyl ester (9CI) (CA INDEX NAME)
 MF C21 H35 N3 O12
 SR CA
 LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL

5 REFERENCES IN FILE CA (1967 TO DATE)
 5 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 123:276025

REFERENCE 2: 107:173781

REFERENCE 3: 103:189386

REFERENCE 4: 102:22672

REFERENCE 5: 101:163360

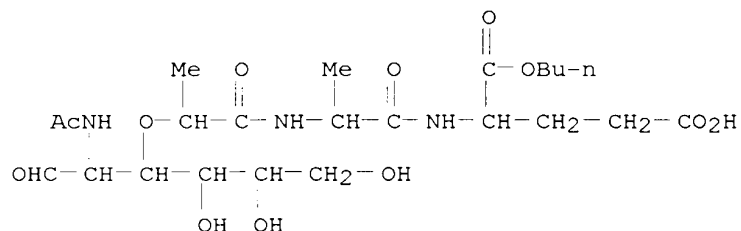
L63 ANSWER 6 OF 24 REGISTRY COPYRIGHT 1998 ACS

RN **90159-44-7** REGISTRY

CN D-Glutamic acid, N-[N-(N-acetylmuramoyl)-L-alanyl]-, 1-butyl ester
 (9CI) (CA INDEX NAME)

MF C23 H39 N3 O12

LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL



3 REFERENCES IN FILE CA (1967 TO DATE)
 3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 123:276025

REFERENCE 2: 113:38702

REFERENCE 3: 100:210439

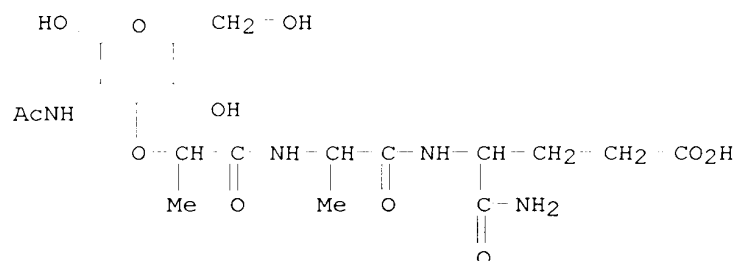
L63 ANSWER 7 OF 24 REGISTRY COPYRIGHT 1998 ACS

RN **87420-93-7** REGISTRY

CN D-.alpha.-Glutamine, N2-[N-(N-acetyl-.alpha.-manno-muramoyl)-L-alanyl]- (9CI) (CA INDEX NAME)

MF C19 H32 N4 O11

LC STN Files: BEILSTEIN*, CA, CAPLUS, TOXLIT, USPATFULL
 (*File contains numerically searchable property data)



2 REFERENCES IN FILE CA (1967 TO DATE)
 2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 112:112072

REFERENCE 2: 99:158826

L63 ANSWER 8 OF 24 REGISTRY COPYRIGHT 1998 ACS
 RN **83869-56-1** REGISTRY
 CN Colony-stimulating factor 2 (9CI) (CA INDEX NAME)
 OTHER NAMES:
 CN Colony-stimulating factor II
 CN CSF 2
 CN GM-CSF
 CN Granulocyte-macrophage colony-simulating factor
 CN Granulocyte-macrophage colony-stimulating activity
 CN Granulocyte-macrophage colony-stimulating factor
 CN Granulocyte-macrophage-inducing factor
 CN Granulocyte-monocyte colony-stimulating factor
 CN Macrophage-granulocyte CSF
 CN Macrophage-granulocyte-colony-stimulating factor
 MF Unspecified
 CI PMS, MAN
 PCT Manual registration
 LC STN Files: ADISINSIGHT, AGRICOLA, AIDSLINE, ANABSTR, BIOBUSINESS,
 BIOSIS, CA, CANCERLIT, CAPLUS, CEN, CHEMCATS, CBNB, CIN, CSCHEM,
 DRUGPAT, DRUGUPDATES, IPA, MEDLINE, MRCK*, PHAR, PROMT, TOXLINE,
 TOXLIT, USPATFULL
 (*File contains numerically searchable property data)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
 5826 REFERENCES IN FILE CA (1967 TO DATE)
 108 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 5839 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:321207

REFERENCE 2: 129:321206

REFERENCE 3: 129:314993

REFERENCE 4: 129:314967

REFERENCE 5: 129:314910

REFERENCE 6: 129:314832

REFERENCE 7: 129:314814

REFERENCE 8: 129:314793

REFERENCE 9: 129:314792

REFERENCE 10: 129:314779

L63 ANSWER 9 OF 24 REGISTRY COPYRIGHT 1998 ACS

RN **81638-45-1** REGISTRY

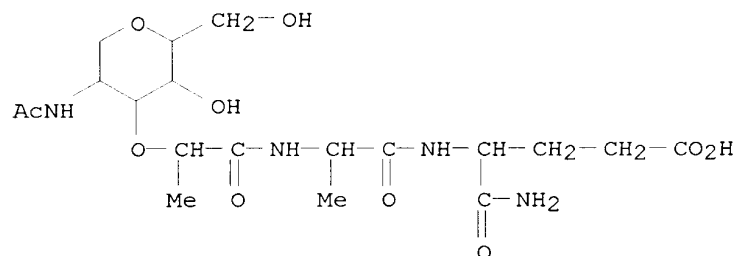
CN D-.alpha.-Glutamine, N2-[N-(N-acetyl-1-deoxymuramoyl)-L-alanyl]-
(9CI) (CA INDEX NAME)

DR 84993-83-9

MF C19 H32 N4 O10

CI COM

LC STN Files: BEILSTEIN*, CA, CAPLUS, TOXLIT, USPATFULL
(*File contains numerically searchable property data)



4 REFERENCES IN FILE CA (1967 TO DATE)

4 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 112:112074

REFERENCE 2: 105:170442

REFERENCE 3: 98:126598

REFERENCE 4: 96:200171

L63 ANSWER 10 OF 24 REGISTRY COPYRIGHT 1998 ACS

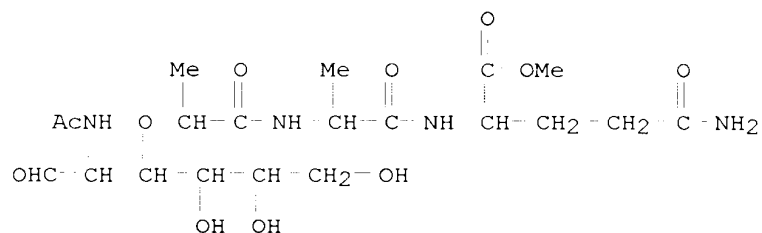
RN **79787-27-2** REGISTRY

CN D-Glutamine, N2-[N-(N-acetylmuramoyl)-L-alanyl]-, methyl ester (9CI)
(CA INDEX NAME)

DR 87349-46-0

MF C20 H34 N4 O11

LC STN Files: CA, CANCERLIT, CAPLUS, EMBASE, MEDLINE, TOXLINE,
TOXLIT, USPATFULL



6 REFERENCES IN FILE CA (1967 TO DATE)

6 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 126:1184

REFERENCE 2: 108:187197

REFERENCE 3: 101:183905

REFERENCE 4: 100:114574

REFERENCE 5: 99:156529

REFERENCE 6: 96:471

L63 ANSWER 11 OF 24 REGISTRY COPYRIGHT 1998 ACS

RN **76498-00-5** REGISTRY

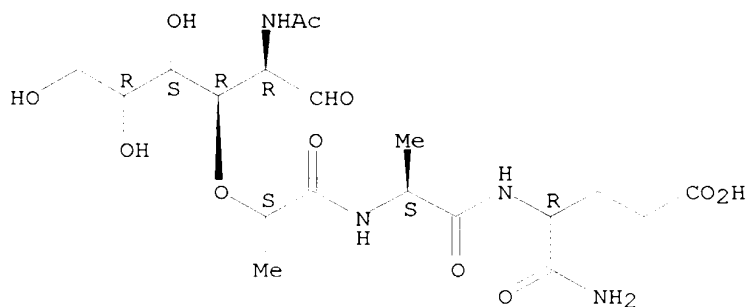
CN D-.alpha.-Glutamine, N2-[N-(N-acetyl-D-galacto-isomuramoyl)-L-alanyl]- (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C19 H32 N4 O11

LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL

Absolute stereochemistry.



2 REFERENCES IN FILE CA (1967 TO DATE)

2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

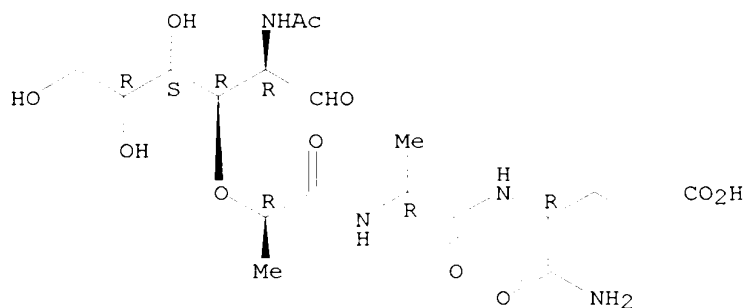
REFERENCE 1: 112:112072

REFERENCE 2: 95:25635

L63 ANSWER 12 OF 24 REGISTRY COPYRIGHT 1998 ACS

RN **76497-96-6** REGISTRY
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 (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C19 H32 N4 O11
 LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL

Absolute stereochemistry.



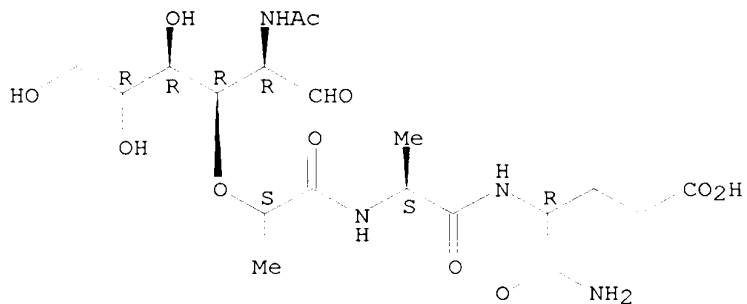
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 2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 112:112072

REFERENCE 2: 95:25635

L63 ANSWER 13 OF 24 REGISTRY COPYRIGHT 1998 ACS
 RN **76465-71-9** REGISTRY
 CN D-.alpha.-Glutamine, N2-[N-(N-acetyl-L-muramoyl)-L-alanyl]- (9CI)
 (CA INDEX NAME)
 FS STEREOSEARCH
 MF C19 H32 N4 O11
 LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL

Absolute stereochemistry.



4 REFERENCES IN FILE CA (1967 TO DATE)
 4 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 122:161318

REFERENCE 2: 112:112072

REFERENCE 3: 95:25635

REFERENCE 4: 94:66050

L63 ANSWER 14 OF 24 REGISTRY COPYRIGHT 1998 ACS

RN **75283-24-8** REGISTRY

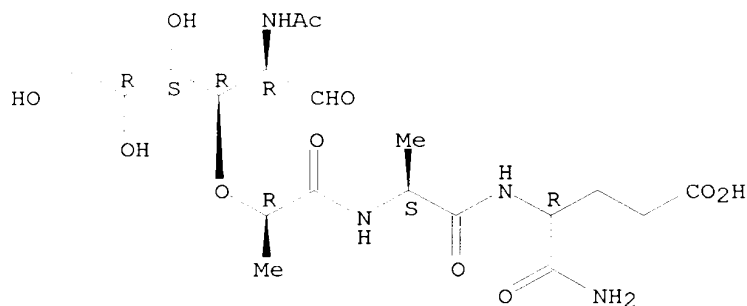
CN D-.alpha.-Glutamine, N2-[N-(N-acetyl-D-galacto-muramoyl)-L-alanyl]-
(9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C19 H32 N4 O11

LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL

Absolute stereochemistry.



9 REFERENCES IN FILE CA (1967 TO DATE)

9 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 112:112072

REFERENCE 2: 107:190333

REFERENCE 3: 100:66286

REFERENCE 4: 98:126607

REFERENCE 5: 97:174449

REFERENCE 6: 96:33017

REFERENCE 7: 96:7051

REFERENCE 8: 95:25635

REFERENCE 9: 93:184104

L63 ANSWER 15 OF 24 REGISTRY COPYRIGHT 1998 ACS

RN **75283-22-6** REGISTRY

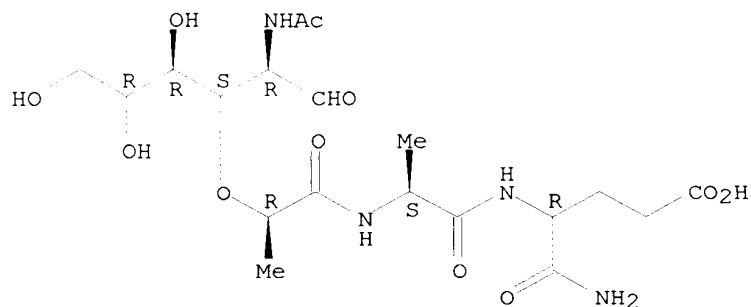
CN D-.alpha.-Glutamine, N2-[N-(N-acetyl-D-allo-muramoyl)-L-alanyl]-
(9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C19 H32 N4 O11

LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL

Absolute stereochemistry.



12 REFERENCES IN FILE CA (1967 TO DATE)
12 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 112:112072

REFERENCE 2: 107:190333

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REFERENCE 4: 103:158639

REFERENCE 5: 100:66286

REFERENCE 6: 98:126607

REFERENCE 7: 97:174449

REFERENCE 8: 96:33017

REFERENCE 9: 96:7051

REFERENCE 10: 95:25635

L63 ANSWER 16 OF 24 REGISTRY COPYRIGHT 1998 ACS

RN **74817-61-1** REGISTRY

CN D-Glutamine, N-(N-acetylmuramoyl)-L-alanyl-, butyl ester (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN D-Glutamine, N2-[N-(N-acetylmuramoyl)-L-alanyl]-, butyl ester

OTHER NAMES:

CN Murabutide

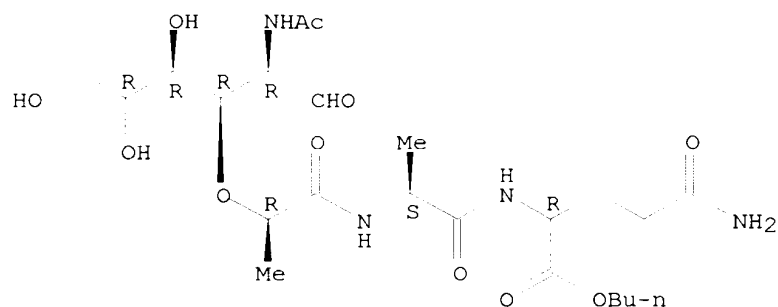
FS STEREOSEARCH

DR 83504-22-7, 87370-60-3

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Other Sources: WHO

Absolute stereochemistry.



96 REFERENCES IN FILE CA (1967 TO DATE)

6 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

96 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 128:226238

REFERENCE 2: 128:30028

REFERENCE 3: 128:10060

REFERENCE 4: 125:265378

REFERENCE 5: 125:123683

REFERENCE 6: 125:76342

REFERENCE 7: 125:55903

REFERENCE 8: 125:26240

REFERENCE 9: 124:340332

REFERENCE 10: 124:317852

L63 ANSWER 17 OF 24 REGISTRY COPYRIGHT 1998 ACS

RN **69351-74-2** REGISTRY

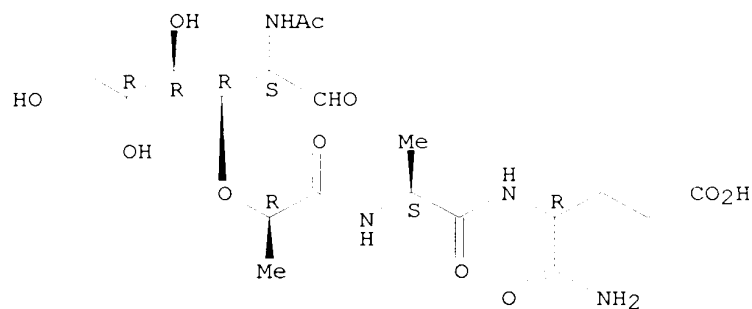
CN D-.alpha.-Glutamine, N2-[N-(N-acetyl-D-manno-muramoyl)-L-alanyl]-
(9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C19 H32 N4 O11

LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL

Absolute stereochemistry.



6 REFERENCES IN FILE CA (1967 TO DATE)
6 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 112:112072

REFERENCE 2: 97:174449

REFERENCE 3: 96:33017

REFERENCE 4: 96:7051

REFERENCE 5: 95:25635

REFERENCE 6: 90:132579

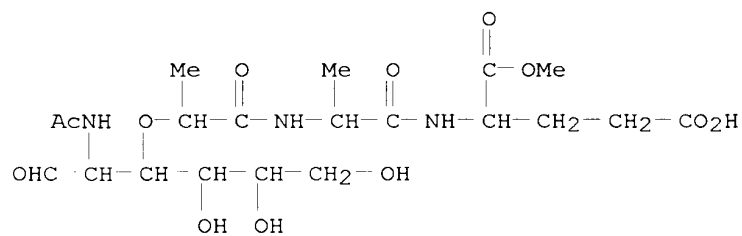
L63 ANSWER 18 OF 24 REGISTRY COPYRIGHT 1998 ACS

RN **63555-62-4** REGISTRY

CN D-Glutamic acid, N-[N-(N-acetylmuramoyl)-L-alanyl]-, 1-methyl ester
(9CI) (CA INDEX NAME)

MF C20 H33 N3 O12

LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL



11 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

11 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 123:276025

REFERENCE 2: 108:137895

REFERENCE 3: 101:50651

REFERENCE 4: 100:210439
 REFERENCE 5: 100:114574
 REFERENCE 6: 93:43645
 REFERENCE 7: 92:215749
 REFERENCE 8: 89:127602
 REFERENCE 9: 89:110389
 REFERENCE 10: 88:87474

L63 ANSWER 19 OF 24 REGISTRY COPYRIGHT 1998 ACS

RN **60355-79-5** REGISTRY

CN D-Glutamic acid, N-[N-(N-acetylmuramoyl)-L-alanyl]-, dimethyl ester
 (9CI) (CA INDEX NAME)

OTHER NAMES:

CN N-Acetylmuramyl-L-alanyl-D-glutamic acid dimethyl ester

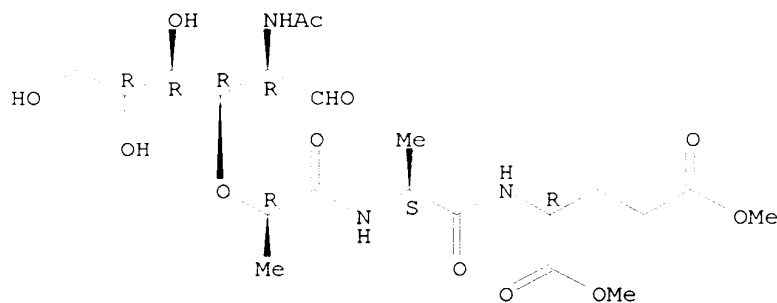
FS STEREOSEARCH

DR 66048-76-8

MF C21 H35 N3 O12

LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL

Absolute stereochemistry.



18 REFERENCES IN FILE CA (1967 TO DATE)

2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

18 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 125:55903
 REFERENCE 2: 123:276025
 REFERENCE 3: 122:23868
 REFERENCE 4: 108:137895
 REFERENCE 5: 104:161623
 REFERENCE 6: 100:114574
 REFERENCE 7: 96:471

REFERENCE 8: 95:204406

REFERENCE 9: 93:43645

REFERENCE 10: 90:136105

L63 ANSWER 20 OF 24 REGISTRY COPYRIGHT 1998 ACS

RN **60355-78-4** REGISTRY

CN D-.alpha.-Glutamine, N-(N-acetylmuramoyl)-L-alanyl-, methyl ester
(9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN D-.alpha.-Glutamine, N2-[N-(N-acetylmuramoyl)-L-alanyl]-, methyl ester

OTHER NAMES:

CN Murametide

CN N-Acetylmuramyl-L-alanyl-D-isoglutamine methyl ester

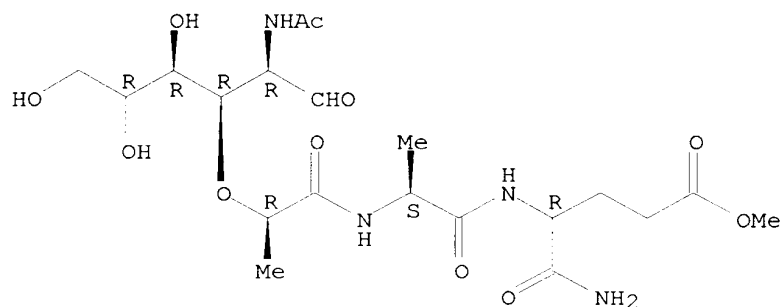
FS STEREOSEARCH

DR 66009-33-4

MF C20 H34 N4 O11

LC STN Files: BIOSIS, CA, CAPLUS, DDFU, DRUGU, TOXLIT, USPATFULL

Absolute stereochemistry.



35 REFERENCES IN FILE CA (1967 TO DATE)

3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

35 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 125:123683

REFERENCE 2: 125:55903

REFERENCE 3: 125:26240

REFERENCE 4: 124:340332

REFERENCE 5: 124:286389

REFERENCE 6: 123:276025

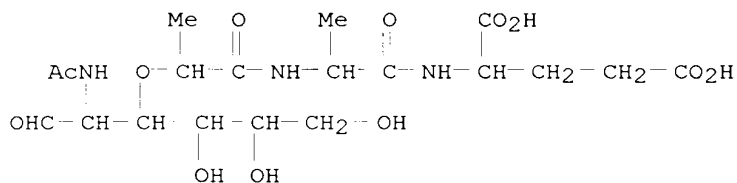
REFERENCE 7: 123:275426

REFERENCE 8: 123:513

REFERENCE 9: 122:312605

REFERENCE 10: 122:48787

L63 ANSWER 21 OF 24 REGISTRY COPYRIGHT 1998 ACS
 RN **59366-95-9** REGISTRY
 CN D-Glutamic acid, N-[N-(N-acetylmuramoyl)-L-alanyl]- (9CI) (CA INDEX NAME)
 OTHER NAMES:
 CN N-Acetylmuramyl-L-alanyl-D-glutamic acid
 DR 66036-56-4
 MF C19 H31 N3 O12
 LC STN Files: CA, CAPLUS, IFICDB, IFIPAT, IFIUDB, TOXLIT, USPATFULL



44 REFERENCES IN FILE CA (1967 TO DATE)
 2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 44 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 124:143034

REFERENCE 2: 123:276025

REFERENCE 3: 116:81895

REFERENCE 4: 113:38702

REFERENCE 5: 109:104367

REFERENCE 6: 108:137895

REFERENCE 7: 107:89474

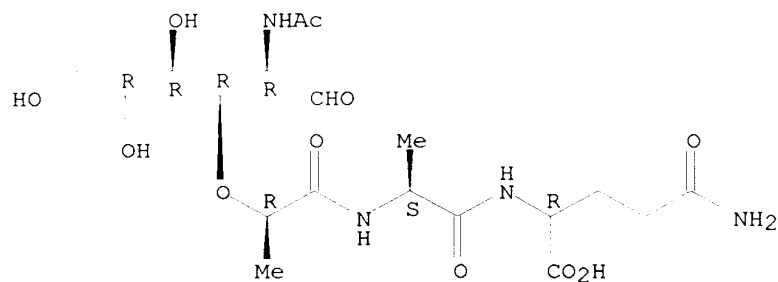
REFERENCE 8: 106:113448

REFERENCE 9: 106:3569

REFERENCE 10: 104:47679

L63 ANSWER 22 OF 24 REGISTRY COPYRIGHT 1998 ACS
 RN **59309-66-9** REGISTRY
 CN D-Glutamine, N-(N-acetylmuramoyl)-L-alanyl- (9CI) (CA INDEX NAME)
 OTHER CA INDEX NAMES:
 CN D-Glutamine, N2-[N-(N-acetylmuramoyl)-L-alanyl]-
 OTHER NAMES:
 CN DV 7401
 CN N-Acetylmuramyl-L-alanyl-D-glutamine
 FS STEREOSEARCH
 MF C19 H32 N4 O11
 CI COM
 LC STN Files: CA, CAPLUS, CHEMCATS, TOXLIT, USPATFULL

Absolute stereochemistry.



31 REFERENCES IN FILE CA (1967 TO DATE)
 2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 31 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 126:224271
 REFERENCE 2: 124:143034
 REFERENCE 3: 120:226704
 REFERENCE 4: 116:81895
 REFERENCE 5: 113:38702
 REFERENCE 6: 109:104367
 REFERENCE 7: 108:187197
 REFERENCE 8: 108:137895
 REFERENCE 9: 107:89474
 REFERENCE 10: 106:113448

L63 ANSWER 23 OF 24 REGISTRY COPYRIGHT 1998 ACS

RN **53678-77-6** REGISTRY

CN D-.alpha.-Glutamine, N-(N-acetylmuramoyl)-L-alanyl- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN D-.alpha.-Glutamine, N2-[N-(N-acetylmuramoyl)-L-alanyl]-

OTHER NAMES:

CN Acetylmuramyl-L-alanyl-D-isoglutamine

CN MDP

CN Muramyl dipeptide

CN N-(Acetylmuramoyl)alanyl-D-isoglutamine

CN N-(Acetylmuramoyl)-L-alanyl-D-isoglutamine

CN N-Acetylmuramyl dipeptide

FS STEREOSEARCH

DR 56769-34-7, 66900-75-2, 66547-81-7, 67461-04-5, 68931-97-5,
 74072-38-1, 75720-23-9, 87349-54-0

MF C19 H32 N4 O11

CI COM

LC STN Files: AGRICOLA, AIDSLINE, BIOBUSINESS, BIOSIS, CA, CANCERLIT,
 CAPLUS, CASREACT, CEN, CHEMCATS, CHEMLIST, CIN, CSCHM, DDFU,

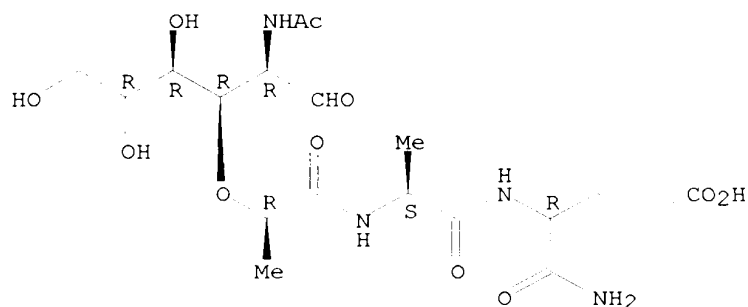
DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*,
MSDS-OHS, NAPRALERT, NIOSHTIC, PHAR, PROMT, RTECS*, TOXLINE,
TOXLIT, USPATFULL, VETU

(*File contains numerically searchable property data)

Other Sources: EINECS**

(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



1194 REFERENCES IN FILE CA (1967 TO DATE)

295 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

1196 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:290431

REFERENCE 2: 129:258969

REFERENCE 3: 129:245466

REFERENCE 4: 129:239903

REFERENCE 5: 129:235685

REFERENCE 6: 129:229679

REFERENCE 7: 129:221081

REFERENCE 8: 129:180079

REFERENCE 9: 129:166193

REFERENCE 10: 129:149242

L63 ANSWER 24 OF 24 REGISTRY COPYRIGHT 1998 ACS

RN **9001-92-7** REGISTRY

CN Proteinase (9CI) (CA INDEX NAME)

OTHER NAMES:

CN Actinase

CN Aquatinase E

CN Arginine esterase

CN AS 10

CN Azocaseinase

CN BAPAase

CN Casein endopeptidase
CN Caseinase
CN DA 10
CN DA 10 (enzyme)
CN Endopeptidase
CN Endopeptidase O
CN Endoprotease
CN Endoproteinase
CN Enzylase K 40
CN Enzylon SAL
CN Enzylon SAL 300
CN Enzymes, proteolytic
CN Esteroproteinase
CN Fibrinase
CN GPR protease
CN Growth-related proteinase
CN Isofloridoside phosphate synthase-activating proteinase
CN Leukase
CN Milk-clotting acid proteinase
CN Newlase A
CN Pathogenesis-related proteinase P 69
CN Prolase
CN Protease
CN Protease P3
CN Protease YP-SS
CN Protein p20 proteinase
CN Protein-cleaving enzymes
CN Proteolytic enzyme
CN Proteopol FP-t
CN Samprose F
CN Tamase
CN Thermoase PS
CN ZY 88
DR 9001-93-8, 9012-23-1, 9040-76-0, 125498-72-8, 125752-86-5,
123779-18-0, 124041-97-0, 120038-39-3, 120038-40-6, 105913-13-1,
118901-82-9, 144906-30-9, 143404-30-2, 143404-41-5, 116267-38-0,
117278-03-2, 117698-27-8, 118390-80-0
MF Unspecified
CI COM, MAN
LC STN Files: AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, CA, CAPLUS,
CASREACT, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CBNB, CIN,
CSCHEM, CSNB, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA,
MSDS-OHS, NAPRALERT, NIOSHTIC, PIRA, PLASPEC*, PROMT, RTECS*,
TOXLINE, TOXLIT, TULSA, USPATFULL, VTB
(*File contains numerically searchable property data)
Other Sources: EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

25882 REFERENCES IN FILE CA (1967 TO DATE)

301 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

25905 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:321213

REFERENCE 2: 129:321174

REFERENCE 3: 129:317991

REFERENCE 4: 129:317981
REFERENCE 5: 129:316287
REFERENCE 6: 129:316217
REFERENCE 7: 129:315584
REFERENCE 8: 129:315368
REFERENCE 9: 129:315330
REFERENCE 10: 129:315288

=> fil hcaplus

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FILE COVERS 1967 - 8 Dec 1998 VOL 129 ISS 24
FILE LAST UPDATED: 8 Dec 1998 (981208/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

This file supports REGISTRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

=> d bib abs hitrn tot 162

L62 ANSWER 1 OF 23 HCAPLUS COPYRIGHT 1998 ACS
AN 1998:527193 HCAPLUS
DN 129:166193
TI Therapeutic treatment and prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix
IN Setterstrom, Jean A.; Van Hamont, John E.; Reid, Robert H.; Jacob, Elliot; Jeyanthi, Ramasubbu; Boedeker, Edgar C.; McQueen, Charles E.; Tice, Thomas R.; Roberts, F. Donald; Friden, Phil
PA United States Dept. of the Army, USA; Van Hamont, John E.; et al.
SO PCT Int. Appl., 363 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	----	-----	-----	-----
PI	WO 9832427	A1	19980730	WO 98-US1556	19980127
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ,				

DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP,
 KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,
 NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR,
 TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU,
 TJ, TM
 RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES,
 FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
 CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
 AU 9863175 A1 19980818 AU 98-63175 19980127
 PRAI US 97-789734 19970127
 WO 98-US1556 19980127
 AB Novel burst-free, sustained release biocompatible and biodegradable
 microcapsules are disclosed which can be programmed to release their
 active core for variable durations ranging from 1-100 days in an aq.
 physiol. environment. The microcapsules are comprised of a core of
 polypeptide or other biol. active agent encapsulated in a matrix of
 poly(lactide/glycolide) copolymer, which may contain a
 pharmaceutically acceptable adjuvant, as a blend of upcapped free
 carboxyl end group and end-capped forms ranging in ratios from 100/0
 to 1/99.
 IT **53678-77-6D**, Muramyl dipeptide, derivs.
 RL: BPR (Biological process); DEV (Device component use); PEP
 (Physical, engineering or chemical process); THU (Therapeutic use);
 BIOL (Biological study); PROC (Process); USES (Uses)
 (prevention of infections with a bioactive material encapsulated
 within a biodegradable-biocompatible polymeric matrix)
 L62 ANSWER 2 OF 23 HCAPLUS COPYRIGHT 1998 ACS
 AN 1998:239318 HCAPLUS
 DN 128:293978
 TI Compositions and methods for treating viral infections
 IN Gelder, Frank B.
 PA Probe International, USA
 SO PCT Int. Appl., 152 pp.
 CODEN: PIXXD2
 DT **Patent**
 LA English
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9815658	A1	19980416	WO 97-US18257	19971010
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG AU 9748131 A1 19980505 AU 97-48131 19971010 PRAI US 96-28194 19961010 WO 97-US18257 19971010 AB Methods and compns. for treatment, diagnosis, and prevention of a virus comprise administering to a patient antibodies which react with regions of viral proteins and result in neutralization of infectivity and inactivation of functionally essential events in the life cycle of the virus. The antibodies recognize viral epitopes which fail to elicit an immune response in man when encountered				

through infection or naturally through the environment. The viral epitope mimics epitope region of **HIV**-1 envelope gp120 external glycoprotein, envelope gp41 transmembrane glycoprotein, reverse transcriptase, **protease** p10 or gag precursor. In a preferred embodiment, the invention provides compns. and methods useful in the treatment and diagnosis of **human immunodeficiency virus (HIV)** infections.

IT **53678-77-6**, Muramyl dipeptide

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (antibodies recognizing **HIV** glycoprotein epitopes or analogs that do not elicit immune response are prepd. for preventing or treating or diagnosing viral or **HIV** infections)

IT **9001-92-7, Protease**

RL: BSU (Biological study, unclassified); BIOL (Biological study) (p10; antibodies recognizing **HIV** glycoprotein epitopes or analogs that do not elicit immune response are prepd. for preventing or treating or diagnosing viral or **HIV** infections)

L62 ANSWER 3 OF 23 HCAPLUS COPYRIGHT 1998 ACS

AN 1997:757027 HCAPLUS

DN 128:13443

TI Preparation of lipophilic muramylpeptide derivatives for treatment of retroviral infection and induction of chemokines

IN Vosika, Gerald J.; Fast, David

PA Endorex Corporation, USA

SO PCT Int. Appl., 46 pp.

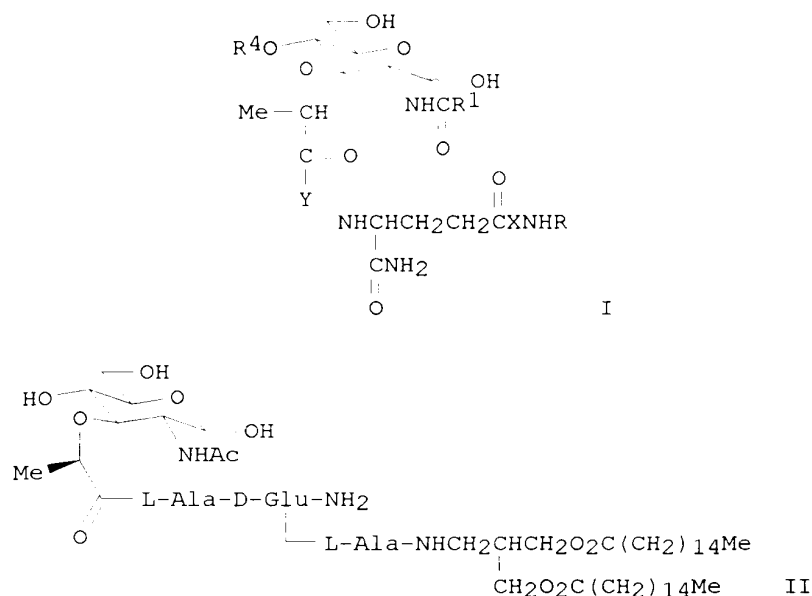
CODEN: PIXXD2

DT **Patent**

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9743308	A1	19971120	WO 97-US8146	19970509
	W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
	AU 9730066	A1	19971205	AU 97-30066	19970509
PRAI	US 96-17248		19960510		
	WO 97-US8146		19970509		
OS	MARPAT 128:13443				
GI					



AB The invention is directed to methods of inducing the release of at least one chemokine by administering an effective amt. of a muramyl dipeptide compd. (MDP compd.) I [R = CH(O₂CR₂)O₂CR₃, CH₂CH(O₂CR₂)CH₂O₂CR₃, CH(CO₂R₅)(CH₂)_nNHCR₆, R₇; R₁ = C₁-9 alkyl; R₂, R₃, R₆, R₇ = independently C₆-30 hydrocarbon contg. 0-4 double bonds; R₄ = H, N-acetylglucosaminyl; R₅ = (CH₂)_nMe, n = 0-22; X = spacer group that does not substantially adversely affect the activity or the toxicity of the MDP compd; Y = single bond, peptide residue contg. 1-10 amino acid groups] to a mammal. Another aspect of the invention is directed to methods of treating retroviral infections, such as **HIV** infections by administering an effective amt. of a muramyl dipeptide compd. to a mammal. The invention is also directed to a pharmaceutical compn. for inducing the release of at least one chemokine and treating retroviral infections, such as **HIV** infections, wherein the pharmaceutical compn. includes an amide linked analog of N-Acetylmuramyl-L-Ala-D-Glu-NH₂. The invention may further include a method of inducing the release of at least one chemokine and a method of treating retroviral infection in a patient by administering an effective amt. of a non-toxic enterotoxin such as ovine toxic shock syndrome toxin (O-TSST) in combination with the MDP compd. Thus, peptide coupling of muramyl dipeptide Mur(NAc)-L-Ala-D-IsoGln-OH (prepn. given) with L-alanine di(palmitoyloxy)propylamide gave analog II as a white powder after purifn. II and a no. of other analogs were tested for chemokine induction and antiviral activity.

IT **53678-77-6P**

RL: BAC (Biological activity or effector, except adverse); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of lipophilic muramylpeptide derivs. for treatment of retroviral infection and induction of chemokines)

L62 ANSWER 4 OF 23 HCAPLUS COPYRIGHT 1998 ACS

AN 1997:684420 HCAPLUS

DN 127:345327

TI Non-dendritic backbone peptide carrier

IN Heegaard, Peter Mikael Helweg; Jakobsen, Palle Hoy

PA Pepresearch A/S, Den.; Heegaard, Peter Mikael Helweg; Jakobsen, Palle Hoy

SO PCT Int. Appl., 261 pp.

CODEN: PIXXD2

DT **Patent**

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9738011	A1	19971016	WO 97-DK146	19970403
	W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
	AU 9725679	A1	19971029	AU 97-25679	19970403
PRAI	DK 96-398		19960403		
	WO 97-DK146		19970403		
AB	The present invention relates to a non-dendritic peptide designed for use as a carrier of an immunogenic substance and/or an immune mediator, a construct of said carrier carrying an immunogenic substance and/or an immune mediator, a process for the prepn. of immunogens with high and predictable immunogenicity which comprise said non-dendritic peptide carrier, use of such immunogens for the prodn. of vaccines and vaccines comprising an immunogenic substance and/or an immune mediator on the peptide carrier. The invention also relates to diagnostic or therapeutic embodiments using the non-dendritic peptide carrier, to diagnostic or therapeutic compns. and to methods for the use thereof in diagnosis of diseases and pregnancy as well as in therapy. The non-dendritic peptide carrier according to the invention comprises 10-50 amino acids capable of forming a secondary structure in a benign buffer after liberation from the solid phase.				
IT	53678-77-6 , Muramyldipeptide				
	RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (non-dendritic backbone peptide carrier for immunogenic peptide, immune mediator or vaccine)				

L62 ANSWER 5 OF 23 HCAPLUS COPYRIGHT 1998 ACS

AN 1997:240684 HCAPLUS

DN 126:224271

TI Non-specific vaccination by D-amino-acid containing compounds

IN Slesarev, Vladimir I.; Efimov, Vladimir A.; Oraevsky, Alexander A.; Slesarev, Alexei I.

PA Slesarev, Vladimir I., USA; Efimov, Vladimir A.

SO PCT Int. Appl., 32 pp.

CODEN: PIXXD2

DT **Patent**

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9705889	A1	19970220	WO 96-US12525	19960731
	W: CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
PRAI	US 95-510737		19950803		
OS	MARPAT 126:224271				
AB	Non-specific vaccination is achieved by administering muramyl or glucosaminylmuramyl di- or tri-peptides with D-amino acid residue in a second or third position from the proximal end. The D-amino acid-contg. muramyl or glucosaminylmuramyl di- or tri-peptides are used as supplement to infant formula or human milk to reduce diarrhea, or administered via oral, vaginal, rectal or topic route to reduce cancer or HIV transmission through sexual contacts. The presence of N-acetyl-D-glucosaminyl-(1.fwdarw.4)-N-acetylmuramyl-L-alanyl-D-isoglutamine (GMDP) in human milk and yoghurt was detd. by antibody capture assay. Administration of GMDP to prevent Clostridium perfringens-assocd. diarrhea in piglets and inhibition of HIV gp120 binding to CD4 receptor by GMDP were also demonstrated. Use of the non-specific anticancer vaccine (GMDP) combined with NMR and ultrasound technol. for its monitoring was also described.				
IT	59309-66-9 , N-Acetylmuramyl-L-alanyl-D-glutamine RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (D-amino acid-contg. muramyl or glucosaminylmuramyl dipeptide or tripeptide as nonspecific vaccine for redn. of diarrhea, cancer or HIV transmission through sexual contact)				

L62 ANSWER 6 OF 23 HCAPLUS COPYRIGHT 1998 ACS
 AN 1996:731868 HCAPLUS
 DN 126:1184
 TI MDP derivatives and conjugates having hematopoietic function stimulating activity
 IN **Bahr, Georges**; Lefrancier, Pierre; Chedid, Louis
 PA **Vacsyn S.A., Fr.**
 SO PCT Int. Appl., 49 pp.
 CODEN: PIXXD2
 DT **Patent**
 LA French

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9631533	A1	19961010	WO 96-FR527	19960405
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
	FR 2732604	A1	19961011	FR 95-4194	19950407
	FR 2732604	B1	19970606		
	CA 2216599	AA	19961010	CA 96-2216599	19960405
	AU 9655046	A1	19961023	AU 96-55046	19960405
	EP 819136	A1	19980121	EP 96-912079	19960405
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRAI FR 95-4194 19950407
 WO 96-FR527 19960405
 OS MARPAT 126:1184
 AB A pharmaceutical compn. for stimulating the hematopoietic function and preventing the myelotoxic side-effects of some treatments, contain at least one water-sol. muramyl peptide deriv. such as Muradimetide (I) or murectasine. I.v. administration of 25 mg I/kg to guinea pigs for 4 days increased the no. of myelocytes from 7x10⁴/mL to 72x10⁴/mL. A soln. of 320 mg 6-O-succinyl-N-acetyl-muramyl-L-alanyl-D-glutamic acid di-Me ester in 10 mL anhyd. DMF was mixed with 0.05 mL of Me morpholine, 0.06 mL of iso-Bu chlorocarbonate, and 267 mg 3'-azido-3'-deoxythymidine and stirred at 15.degree. for 24 h to obtain 6-O-(succinyl-3'-azido-3'-deoxythymidine)-N-acetyl-muramyl-L-alanyl-D-glutamic acid di-Me ester which was purified (yield:50%).
 IT **79787-27-2**
 RL: RCT (Reactant)
 (MDP derivs. and conjugates having hematopoietic function stimulating activity)

L62 ANSWER 7 OF 23 HCAPLUS COPYRIGHT 1998 ACS
 AN 1996:694251 HCAPLUS
 DN 125:326402
 TI An immunoreactive conjugate, method for its preparation, antibodies to the conjugate and a pharmaceutical composition and diagnostic device containing them
 IN Maes, Roland
 PA Anda Biologicals S.A., Fr.
 SO Eur. Pat. Appl., 19 pp.
 CODEN: EPXXDW
 DT **Patent**
 LA French
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 736770	A2	19961009	EP 96-870042	19960401
	EP 736770	A3	19970502		
	R: BE, DE, FR, GB, IT				
	BE 1009230	A6	19970107	BE 95-316	19950405
	BE 1009917	A6	19971104	BE 96-113	19960208
PRAI	BE 95-316		19950405		
	BE 96-113		19960208		
AB	An immunoreactive conjugate is disclosed which contains 1 or more haptens consisting of a sulfhydryl group and one of the following: amino acids, carbohydrates, amino carbohydrates, phosphatidylinositol, sphingosine, and their nitrosyl, acyl, or acetyl derivs., the haptens being coupled to a protein with a mol. wt. >8000 Kd and/or a solid support by a coupling agent capable of binding to the sulfhydryl group of the hapten. Thus, NO-cysteine and NO-N-acetyl-L-cysteine conjugates with albumin were prepd., and birds and mammals were vaccinated. IgG and IgM class antibodies specific for N-acetyl-L-cysteine were detected in the subjects. Addnl. analyses demonstrated that many HIV -pos. patients have IgG specific for acetyl-cysteine. Pharmaceutical compns. using these immunoreactive conjugates can be used in the prevention and/or treatment of autoimmunity, AIDS , cancer, tuberculosis and a variety of other diseases.				
IT	53678-77-6 , N-Acetyl-muramyl-L-alanyl-D-isoglutamine 53678-77-6D , N-Acetyl-muramyl-L-alanyl-D-isoglutamine,				

nitrosyl derivs.

RL: BPR (Biological process); THU (Therapeutic use); BIOL

(Biological study); PROC (Process); USES (Uses)

(in prepn. of immunoreactive conjugates with haptens and carrier protein, antibodies to them, and application in diagnosis and treatment of disease)

L62 ANSWER 8 OF 23 HCAPLUS COPYRIGHT 1998 ACS

AN 1996:483722 HCAPLUS

DN 125:140546

TI Induction of cytotoxic T-lymphocyte responses

IN Raychaudhuri, Syamal; Rastetter, William H.

PA Idec Pharmaceuticals Corporation, USA

SO PCT Int. Appl., 72 pp.

CODEN: PIXXD2

DT **Patent**

LA English

FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9617863	A1	19960613	WO 95-US15433	19951129
	W:	AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK			
	RW:	KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
	US 5709860	A	19980120	US 94-351001	19941207
	AU 9644104	A1	19960626	AU 96-44104	19951129
	EP 801656	A1	19971022	EP 95-942921	19951129
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE			
	BR 9509872	A	19971125	BR 95-9872	19951129
	NO 9702521	A	19970806	NO 97-2521	19970603
	FI 9702431	A	19970606	FI 97-2431	19970606
PRAI	US 94-351001		19941207		
	US 91-735069		19910725		
	US 92-919787		19920724		
	WO 95-US15433		19951129		

AB Methods and compns. useful for inducing a cytotoxic T-lymphocyte response (CTL) in a human or domesticated or agriculturally important animal. The method includes the steps of providing the antigen to which the CTL response is desired and providing an antigen formulation which comprises, consists, or consists essentially of two or more of a stabilizing detergent, a micelle-forming agent, and an oil. This antigen formulation is preferably lacking in an immunostimulating peptide component, or has sufficiently low levels of such a component that the desired CTL response is not diminished. This formulation is provided as a stable oil-in-water emulsion.

IT **53678-77-6**, Muramyl dipeptide

RL: MOA (Modifier or additive use); USES (Uses)

(compn. contg. antigen and detergent and micelle-forming agent and oil for induction of cytotoxic T lymphocyte)

L62 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 1998 ACS

AN 1996:440899 HCAPLUS

DN 125:96040

TI Immunogenic compositions solubilised in a hydrophobic solvent
 IN New, Roger Randal Charles
 PA Cortecs Limited, UK
 SO PCT Int. Appl., 30 pp.
 CODEN: PIXXD2

DT **Patent**
 LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9614871	A1	19960523	WO 95-GB2675	19951114
	W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2205083	AA	19960523	CA 95-2205083	19951114
	AU 9538534	A1	19960606	AU 95-38534	19951114
	EP 792165	A1	19970903	EP 95-936690	19951114
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 10508834	T2	19980902	JP 95-515847	19951114
	FI 9702054	A	19970514	FI 97-2054	19970514
	NO 9702219	A	19970711	NO 97-2219	19970514
PRAI	GB 94-22990		19941115		
	WO 95-GB2675		19951114		

AB An immunogenic compn. comprising an immunogen solubilised, or otherwise distributed, in a hydrophobic solvent in the absence of a hydrophilic phase. Preferably, the immunogenic compn. is provided as an oral vaccine. Thus, 40 .mu.L of tetanus toxoid (5 mg/mL) was added to 1 mL dispersion of 100 mg/mL soya phosphatidyl choline and the mixt. was lyophilized overnight, followed by addn. of 1 mL of oleic acid to obtain a crystal clear soln. Mice were administered 100 .mu.L of above soln. either s.c. or through an intragastric tube. Antibody levels against tetanus antigen after two wk was much more than controls.

IT **53678-77-6**, Muramyldipeptide
 RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (immunogenic compns. solubilised in a hydrophobic solvent)

L62 ANSWER 10 OF 23 HCAPLUS COPYRIGHT 1998 ACS
 AN 1996:369794 HCAPLUS
 DN 125:26240
 TI Muramyl peptide compositions for inhibiting HIV replication
 IN **Bahr, Georges**
 PA **Vacsyn S.A., Fr.**
 SO PCT Int. Appl., 21 pp.
 CODEN: PIXXD2

DT **Patent**
 LA French

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9609837	A1	19960404	WO 95-FR1239	19950926

$$\begin{array}{c}
 \text{OH} \quad \text{NHCOMe} \\
 | \quad | \\
 \text{HO}-\text{CH}_2-\text{CH}-\text{CH}-\text{CH}-\text{CHO} \\
 | \quad | \quad | \\
 \text{OH} \quad \text{O} \quad \text{CO}-\text{X}-\text{Glu}(\text{OR}^2)\text{OR}^1 \\
 | \\
 \text{R}
 \end{array}$$

I

IT 53678-77-6 59366-95-9 60355-78-4
63555-62-4 74817-61-1 90159-44-7
92512-64-6

IT 60355-79-5
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(muramyl peptide diesters in oral form as immunostimulating
agents)

LA English

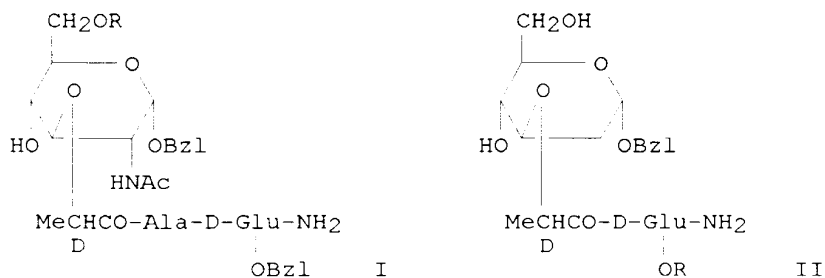
CODEN: CEXIAL; ISSN: 0009-9104

PB Blackwell
 DT Journal
 LA English

AB Since the identification of the **HIV** virus, important advances have been achieved in the definition of potential subunit vaccines. The authors investigated the immunogenicity of a recombinant gp160 antigen and of two gp41 peptides from **HIV** -1LAI assocd. with 7 different adjuvant formulations in squirrel monkeys. All animals were immunized twice with gp160 and then with a gp41 peptide using the same formulation. All adjuvants used led to a subsequent antibody response against gp160, and 55% of the animals immunized developed anti-gp160 antibodies that could neutralize the virus in vitro. Specific anti-gp41 antibody response was also obsd. Results obtained underlined the key role of the adjuvant formulation in the antibody response against a given part of the immunogen, and indicate that such immunogenicity-related investigation can be carried out conveniently in the squirrel monkey *Saimiri sciureus*.

IT **53678-77-6**, Muramyl dipeptide
 RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (immunogenicity of **HIV**-1 gp160 and env peptides in squirrel monkey *Saimiri sciureus* using alumina and exptl. adjuvants)

L64 ANSWER 4 OF 7 HCAPLUS COPYRIGHT 1998 ACS
 AN 1995:21229 HCAPLUS
 DN 122:81977
 TI A new class of antitumor agents: conjugates of MDP and acridine/acridone derivatives
 AU Kolodziejczyk, A. M.; Dzierzbicka, K.; Kolodziejczyk, A. S.
 CS Dep. Org. Chem., Tech. Univ. Gdansk, Gdansk, PL 80-952, Pol.
 SO Pol. J. Chem. (1994), 68 1023-9
 CODEN: PJCHDQ; ISSN: 0137-5083
 DT Journal
 LA English
 GI



AB The synthesis of title muramyl dipeptide (MDP) conjugates I (R = acridine or acridone derivs.) and II has been described. In conjugates I, the hydroxyl group at C6 of the muramyl moiety was

- acylated with acridine carboxy derivs., whereas conjugates II were formed by esterification of isoglutamine carboxyl group with hydroxy derivs. of acridine. The results of the antitumor and anti-**HIV** assays for some of the conjugates are also presented.
- IT **53678-77-6DP**, Muramyl dipeptide, acridine/acridone conjugates
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation) (prepn. of muramyl dipeptide conjugates with acridine/acridone derivs. as antitumor agents)
- L64 ANSWER 5 OF 7 HCAPLUS COPYRIGHT 1998 ACS
AN 1994:603135 HCAPLUS
DN 121:203135
TI Anti-**HIV** and anticancer activity of MDP and acridine derivative conjugates
AU Dzierzbicka, Krystyna; Kolodziejczyk, Aleksander M.; Sosnowska, Danuta; Mysliwski, Andrzej
CS Dep. Organic Chemistry, Technical Univ. of Gdansk, Gdansk, PL-80-952, Pol.
SO Pept. 1992, Proc. Eur. Pept. Symp., 22nd (1993), Meeting Date 1992, 889-90. Editor(s): Schneider, Conrad H.; Eberle, Alex N. Publisher: ESCOM, Leiden, Neth.
CODEN: 60LUAN
DT Conference
LA English
AB Taking into account both the immunostimulatory and synergistic properties of muramyl dipeptide (MDP) and anticancer potency of acridine/acridone derivs., the authors decided to conjugate these compds. covalently. Resulting conjugates exhibit substantial anticancer and anti-**HIV** activities and their toxicity is considerably reduced compared to the acridine counterparts.
- IT **53678-77-6D**, Muramyl dipeptide, conjugates with acridine derivs.
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (anti-**HIV** and anticancer activity of)
- L64 ANSWER 6 OF 7 HCAPLUS COPYRIGHT 1998 ACS
AN 1994:577166 HCAPLUS
DN 121:177166
TI Efficacy of inactivated whole **HIV**-2 vaccines with various adjuvants in cynomolgus monkeys
AU Putkonen, Per; Nilsson, Charlotta; Walther, Lilian; Ghavamzadeh, Lili; Hild, Kerstin; Broliden, Kristina; Biberfeld, Gunnel; Thorstensson, Rigmor
CS Department Immunology, Swedish Institute Infectious Disease Control, Stockholm, Swed.
SO J. Med. Primatol. (1994), 23(2-3), 89-94
CODEN: JMPMAO; ISSN: 0047-2565
DT Journal
LA English
AB Twenty-one cynomolgus monkeys were immunized with whole inactivated **HIV**-2 preps. administered with various adjuvants (incomplete Freund's adjuvant, Alum, Ribl, MDP, or Iscoms) and challenged with 10 or 100 MID50 of a homologous monkey-cell grown, cell-free **HIV**-2.. Seven animals were completely protected against infection, three showed reduced virus replication. The vaccines elicited neutralizing and ADCC antibodies; the titers did

L67 ANSWER 1 OF 1 REGISTRY COPYRIGHT 1998 ACS

RN **61136-12-7** REGISTRY

CN D-.alpha.-Glutamine, N-(N-acetylnormuramoyl)-L-alanyl- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN D-.alpha.-Glutamine, N2-[N-(N-acetylnormuramoyl)-L-alanyl]-

OTHER NAMES:

CN Almutide

CN CGP 11637

CN Desmethylnuramyl dipeptide

CN N-Acetyl desmethylnuramyl-L-alanyl-D-isoglutamine

CN N-Acetylnuramyl-L-alanyl-D-isoglutamine

FS STEREOSEARCH

DR 98725-10-1, 68426-50-6, 72768-58-2, 84227-98-5, 87349-50-6

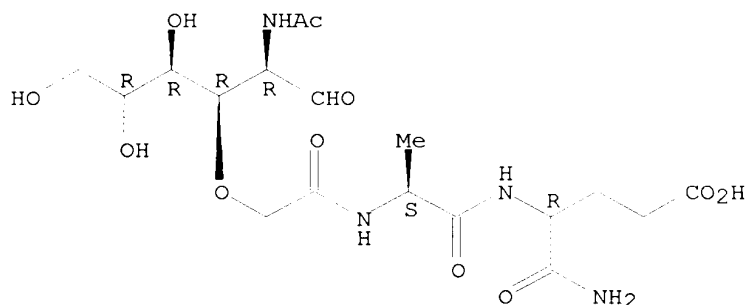
MF C18 H30 N4 O11

CI COM

LC STN Files: BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CANCERLIT, CAPLUS, CASREACT, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, MEDLINE, TOXLIT, USAN, USPATFULL

(*File contains numerically searchable property data)

Absolute stereochemistry.



74 REFERENCES IN FILE CA (1967 TO DATE)

3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

74 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:301384

REFERENCE 2: 128:304812

REFERENCE 3: 122:161318

REFERENCE 4: 121:18008

REFERENCE 5: 120:267865

REFERENCE 6: 118:167134

REFERENCE 7: 118:57798

REFERENCE 8: 118:16298

DT Journal
 FS 004 Microbiology
 026 Immunology, Serology and Transplantation
 037 Drug Literature Index
 038 Adverse Reactions Titles
 LA English
 SL English
 AB Studies indicate that adjuvant formulations based on liposomes, nontoxic lipid A, and muramyl peptide derivatives are safe and effective for vaccine use. Future research on the immunobiology of these adjuvants as well as the mechanisms by which adjuvants can alter the quality of immune responses may play an important role in determining their efficacy in malaria vaccines.
 CT EMTAGS: infection (0310); therapy (0160); prevention (0165); mammal (0738); human (0888); nonhuman (0777); human experiment (0104); oral drug administration (0181); subcutaneous drug administration (0183); intramuscular drug administration (0184); intravenous drug administration (0182); intradermal drug administration (0176); conference paper (0061); adverse drug reaction (0198); iatrogenic disease (0300)
 Medical Descriptors:
 *malaria: DT, drug therapy
 *malaria: PC, prevention
 *vaccination
 *immunobiology
 drug formulation
 drug design
 immunogenicity
 drug safety
 drug activity
 drug efficacy
 antibody response
 drug tolerance
 side effect
 human
 nonhuman
 clinical trial
 phase 1 clinical trial
 oral drug administration
 subcutaneous drug administration
 intramuscular drug administration
 intravenous drug administration
 intradermal drug administration
 conference paper
 Drug Descriptors:
 *malaria vaccine: CT, clinical trial
 *malaria vaccine: DT, drug therapy
 *malaria vaccine: PR, pharmaceuticals
 *immunological adjuvant: PR, pharmaceuticals
 *liposome: PR, pharmaceuticals
 *muramyl dipeptide derivative: PR, pharmaceuticals
 *lipid a: PR, pharmaceuticals
 aluminum potassium sulfate: PR, pharmaceuticals
 phosphoryl lipid a: AE, adverse drug reaction
 phosphoryl lipid a: CT, clinical trial
 phosphoryl lipid a: TO, drug toxicity
 phosphoryl lipid a: PR, pharmaceuticals
 lipid a derivative: TO, drug toxicity
 lipid a derivative: PR, pharmaceuticals

saponin: PR, pharmaceuticals
 iscom: PR, pharmaceuticals
murabutide: PR, pharmaceuticals
 muroctasin: PR, pharmaceuticals
 n acetylmuramylalanyl dextro isoglutaminylalanyl
 dipalmitoylphosphatidylethanolamine: PR, pharmaceuticals
 squalene: PR, pharmaceuticals
 bacterium lipopolysaccharide: TO, drug toxicity
 bacterium lipopolysaccharide: PR, pharmaceuticals
 glucosamine derivative: TO, drug toxicity
 glucosamine derivative: PR, pharmaceuticals
 sporozoite vaccine: AE, adverse drug reaction
 sporozoite vaccine: CT, clinical trial
 sporozoite vaccine: PR, pharmaceuticals
 cell wall skeleton: PR, pharmaceuticals
 freund adjuvant: PR, pharmaceuticals
 membrane antigen
 cord factor: PR, pharmaceuticals
 hepatitis a vaccine: PR, pharmaceuticals
 influenza vaccine: PR, pharmaceuticals
 tetanus toxoid: AE, adverse drug reaction
 tetanus toxoid: PR, pharmaceuticals
 bacterial protein: AE, adverse drug reaction
 bacterial protein: PR, pharmaceuticals
human immunodeficiency virus vaccine: PR, pharmaceuticals
 unindexed drug
 merozoite surface antigen 1: PR, pharmaceuticals
 rhoptry associated protein 1: PR, pharmaceuticals
 serine repeat antigen: PR, pharmaceuticals
 RN 95991-05-2; 10043-67-1; 88598-53-2; 8047-15-2; **74817-61-1**;
 78113-36-7; 83461-56-7; 111-02-4; 7683-64-9; 9007-81-2; 61512-20-7;
 93384-51-1
 CN (1) Mf 59; (2) Detox
 CO (1) Ciba geigy (Switzerland); (2) Ribl (United States)

=> fil aidslines

FILE 'AIDSLINE' ENTERED AT 09:21:10 ON 08 DEC 1998

FILE COVERS 1980 TO 25 NOV 1998 (19981125/ED)

Aidslines has been reloaded with 1998 MeSH headings. See HELP RLOAD
 for details.

This file contains CAS Registry Numbers for easy and accurate
 substance identification.

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L76 ANSWER 1 OF 38 AIDSLINE
 AN 1998:17871 AIDSLINE
 DN ICA12-98392561
 TI Inhibition of HIV-1 replication in reservoir cells by the safe
 immunomodulator **Murabutide**.
 AU Bahr G; Darcissac E; Grau O; Truong M J; Dewulf J; Debard C; Capron
 A
 CS Institut Pasteur de Lille, INSERM U167, France.
 SO Int Conf AIDS, (1998). Vol. 12, pp. 349 (Abstract No. 22424).

CY Switzerland
DT Abstract
FS ICA12
LA English
EM 199812
AB OBJECTIVES: To assess the efficacy of the clinically-acceptable immunomodulator **Murabutide**, a butyl ester derivative of MDP, on the inhibition of HIV replication in monocyte-derived macrophages (MDM) and dendritic cells (MDDC). METHODS: Acutely infected MDMs and MDDCs with M-tropic HIV-1 isolates, were maintained in the absence or presence of **Murabutide**. Reverse transcriptase (RT) or P24 levels in culture supernatants were evaluated 7-21 days post-infection. Proviral DNA and viral mRNA were quantified in infected cells using polymerase chain reaction (PCR) and RT-PCR respectively. The levels of secreted cytokines were also tested by specific ELISA kits. RESULTS: Addition of **Murabutide** to infected MDMs and DCs resulted in 60-100% inhibition of viral replication in cultures from 10 different donors. This effect was found to be mediated, in part, by the induction of high levels of HIV-suppressing beta chemokines, MIP-1 alpha, MIP-1 beta and RANTES. In addition, cells stimulated with **Murabutide** immediately after infection presented highly reduced levels of proviral DNA at the 24 hour period. Analysis of the levels of unspliced and singly-spliced viral mRNA in 8-12 days infected cells showed over 90% inhibition of viral transcripts in **Murabutide**-treated cultures. This inhibitory effect of **Murabutide** was also evident in reservoir cells acutely infected with primary HIV-1 isolates. The safe synthetic immunomodulator **Murabutide** exerts potent HIV-suppressing activity in reservoir cells and is currently being evaluated as an adjunct to antiretroviral therapy.

CT Check Tags: Human
*Acetylmuramyl-Alanyl-Isoglutamine: AA, analogs & derivatives
Acetylmuramyl-Alanyl-Isoglutamine: PD, pharmacology
*Adjuvants, Immunologic: PD, pharmacology
Cells, Cultured
*Dendritic Cells: VI, virology
*HIV Infections: DT, drug therapy
*HIV Infections: IM, immunology
HIV Infections: VI, virology
*HIV-1: DE, drug effects
*HIV-1: PH, physiology
*Macrophages: VI, virology
Virus Replication: DE, drug effects

RN 53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine);
74817-61-1 (N-acetylmuramyl-alanylglutamine-n-butyl ester)

CN 0 (Adjuvants, Immunologic)

L76 ANSWER 2 OF 38 AIDSLINE
AN 1998:9001 AIDSLINE
DN MED-98234020
TI Involvement of T cells in enhanced resistance to Klebsiella pneumoniae septicemia in mice treated with liposome-encapsulated muramyl tripeptide phosphatidylethanolamine or gamma interferon.
AU ten Hagen T L; van Vianen W; Savelkoul H F; Heremans H; Buurman W A; Bakker-Woudenberg I A
CS Department of Clinical Microbiology and Antimicrobial Therapy, Erasmus University Rotterdam, The Netherlands.

tenhagen@heel.fgg.eur.nl

SO INFECTION AND IMMUNITY, (1998). Vol. 66, No. 5, pp. 1962-7.
Journal code: GO7. ISSN: 0019-9567.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

FS MED; Priority Journals; Cancer Journals

LA English

OS MEDLINE 98234020

EM 199807

AB We have previously shown that prophylactic administration of the liposome-encapsulated immunomodulating agents muramyl tripeptide phosphatidylethanolamine (MTPPE) and gamma interferon (IFN-gamma) results in strongly increased survival of mice from a normally lethal septicemia with *Klebsiella pneumoniae*. It was anticipated that the treatment acts on macrophages and nonspecifically augments host resistance to various infections. In the present study, we provide evidence for a key role for T cells in host defense potentiation by the liposomal immunomodulators toward *K. pneumoniae* septicemia. It is shown that both CD4 and CD8 cells are important in immunomodulation, most likely due to production of IFN-gamma. Depletion of circulating IFN-gamma resulted in strong reduction of the antimicrobial host defense activation. Administration of interleukin-10 resulted in decreased antimicrobial host defense activation by liposomal immunomodulators. Moreover, administration of liposomal immunomodulators was shown to induce predominantly T-helper type 1 (Th1) cell populations in the spleen. These findings indicate that immunomodulation with liposomal MTPPE and IFN-gamma favors Th1 and NK cell activation.

CT Check Tags: Animal; Female; Support, Non-U.S. Gov't
***Acetylmuramyl-Alanyl-Isoglutamine: AA, analogs & derivatives**
Acetylmuramyl-Alanyl-Isoglutamine: AD, administration & dosage
 *Adjuvants, Immunologic: AD, administration & dosage
 *Bacteremia: IM, immunology
 Histocompatibility Antigens Class II: AN, analysis
 *Interferon Type II: AD, administration & dosage
 Interleukin-10: PD, pharmacology
 *Klebsiella pneumoniae
 *Klebsiella Infections: IM, immunology
 Liposomes
 Mice
 Mice, Inbred C57BL
 *Phosphatidylethanolamines: AD, administration & dosage
 *T-Lymphocytes: IM, immunology
 Th1 Cells: IM, immunology
 Th2 Cells: IM, immunology

RN 130068-27-8 (Interleukin-10); **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine)**; 82115-62-6 (Interferon Type II); 83461-56-7 (CGP 19835 A)

CN 0 (Adjuvants, Immunologic); 0 (Histocompatibility Antigens Class II); 0 (Liposomes); 0 (Phosphatidylethanolamines)

L76 ANSWER 3 OF 38 AIDSLINE

AN 1997:23069 AIDSLINE

DN MED-97448354

TI Study of the adjuvant activity of new MDP derivatives and purified saponins and their influence on HIV-1 replication in vitro.

AU Krivorutchenko Y L; Andronovskaja I B; Hinkula J; Krivoshein Y S;

CT Check Tags: Animal; Female; In Vitro
***Acetylmuramyl-Alanyl-Isoglutamine: AA, analogs & derivatives**
Acetylmuramyl-Alanyl-Isoglutamine: AD, administration & dosage
*Adjuvants, Immunologic: AD, administration & dosage
*Antigens: AD, administration & dosage
*Cytotoxicity, Immunologic
*CD8-Positive T-Lymphocytes: IM, immunology
Immunization
Mice
Mice, Inbred C57BL
Ovalbumin: IM, immunology
Solubility
Tumor Cells, Cultured

RN **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine); 70280-03-4**
(N-acetyl-beta-glucosaminyl-N-acetylmuramyl-alanylisoglutamine);
9006-59-1 (Ovalbumin)

CN 0 (Adjuvants, Immunologic); 0 (Antigens)

L76 ANSWER 6 OF 38 AIDSLINE
AN 1996:436 AIDSLINE
DN MED-96020392
TI Alteration of spleen lymphocyte populations in rats with arthritis induced by muramyl dipeptide analogue or complete adjuvant.
AU Sugawara T; Miyamoto M; Takada S; Nomura M; Kato M
CS Drug Safety Research Center, Daiichi Pharmaceutical Co., Ltd., Tokyo, Japan.
SO INTERNATIONAL JOURNAL OF TISSUE REACTIONS, (1995). Vol. 17, No. 1, pp. 5-13.
Journal code: GTG. ISSN: 0250-0868.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
FS MED; Priority Journals
LA English
OS MEDLINE 96020392
EM 199603
AB To examine the involvement of lymphocytes in the development of MDP-Lys(L18)-induced arthritis (MIA) in rats and the exacerbation of MIA by cyclosporin A (CsA), we analysed the spleen lymphocyte subset using monoclonal antibodies and flow cytometry during the development of arthritis and compared the results with those found in adjuvant-induced arthritis (AIA). Subcutaneous injection of MDP-Lys(L18) 4 mg/kg to male Lewis rats for 14 days caused very slight and quite clear increases in tarsal joint thickness on days 8 and 15, respectively. This increase was significantly enhanced by co-administration of CsA 10 mg/kg on both of these days. Adjuvant intracutaneously injected once increased the thickness only on day 15, and this was completely inhibited by CsA. The populations of CD4+ and CD8+ cells were increased and decreased, respectively, increasing the CD4+/CD8+ ratio, from day 8 in MIA. CsA enhanced the MDP-Lys(L18)-induced changes in these populations and caused additional decreases in the number of CD5+ cells. Only the CD4+ cell population was increased on day 15 in AIA, and this increase was inhibited by CsA. These results suggest that the spleen lymphocyte subsets in MIA have a different role from those in AIA, and that the contribution of enhancement of the subset changes to the exacerbating effect of CsA on MIA.

CT Check Tags: Animal; Male

*Squalene: AD, administration & dosage
Vaccines, Synthetic: AD, administration & dosage
*Vaccines, Synthetic: IM, immunology

RN 111-02-4 (Squalene); **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine)**; 83461-56-7 (CGP 19835 A)

CN 0 (Adjuvants, Immunologic); 0 (AIDS Vaccines); 0 (HIV Antibodies); 0 (HIV Envelope Protein gp120); 0 (MF59 oil emulsion); 0 (Phosphatidylethanolamines); 0 (Polysorbates); 0 (Vaccines, Synthetic)

L76 ANSWER 9 OF 38 AIDSLINE

AN 1994:8699 AIDSLINE

DN MED-94293161

TI Effect of MTP-PE liposomes and interleukin-7 on induction of antibody and cell-mediated immune responses to a recombinant HIV-envelope protein.

AU Bui T; Dykers T; Hu S L; Faltynek C R; Ho R J

CS Department of Pharmaceutics, University of Washington, Seattle 98195

NC AI 31854 (NIAID)

SO JOURNAL OF ACQUIRED IMMUNE DEFICIENCY SYNDROMES, (1994). Vol. 7, No. 8, pp. 799-806.
Journal code: JOF. ISSN: 0894-9255.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

FS MED; Priority Journals

LA English

OS MEDLINE 94293161

EM 199410

AB We investigated the ability of human recombinant interleukin-7 (IL-7) to enhance the immune responses of mice vaccinated with either the alum-associated or liposome-formulated recombinant human immunodeficiency virus (HIV)-envelope protein, env-2-3SF2 (a nonglycosylated denatured gp 120 of HIV-1SF2 produced in genetically engineered yeast). Pathogen-free (C3H) mice were vaccinated on days 0, 14, and 28 with 10 micrograms of either the alum-associated env-2-3SF2 or liposome-formulated env-2-3SF2, both containing a lipophylic muramyl tripeptide, MTP-PE. Liposome-formulated IL-7 (5 micrograms/mouse) or empty liposomes were given on days 7, 14, 21, and 28. Antibody response against the immunized antigen, evaluated on day 21 and day 35 or 42, showed that liposome-formulated antigen induced higher antibody titer than did alum-associated antigen, and these antibody responses can be enhanced by concurrent administration of IL-7 liposomes. Spleen cells were harvested on day 21 and day 35 or 42 to evaluate cytotoxic T lymphocyte responses directed against autologous cells infected with vaccinia virus-expressing HIV-envelope protein. Mice treated with liposome-formulated antigen expressed the highest cytotoxic t-lymphocyte (CTL) activity, regardless of whether IL-7 liposome was given as an immune potentiator. In contrast, spleen cells from mice vaccinated with alum-associated antigen exhibited minimal CTL response, which was enhanced by concurrent IL-7 liposome treatment. Collectively, IL-7 liposome treatment enhanced the antibody production of the alum-associated or liposome-formulated env-2-3SF2, whereas its enhancement of CTL activity was detected only in mice vaccinated with alum-associated antigen.

CT Check Tags: Animal; Support, U.S. Gov't, P.H.S.
***Acetylmuramyl-Alanyl-Isoglutamine: AA, analogs & derivatives**

+ FA). All of the monkeys became infected after intravenous challenge. However, 16 days following infection, viral antigenemia was reduced in both groups of vaccinates compared to controls. After 23 days antigenemia in the gp110 + SAF-M group remained at the same level as on day 16, whereas antigenemia in the gp140 + FA group was significantly reduced further than the level observed on day 16. Both vaccines induced blastogenic responses in PBMC cultures stimulated with rgp140, which decreased after repeated immunizations. Both vaccines induced high ELISA titers of IgG antibody against rgp140 that were equivalent to the titers in asymptomatic long-term survivors (LTSS). gp110 +/- SAF-M induced high titers of neutralizing antibody. In contrast, gp140 + FA failed to induce neutralizing antibody, suggesting that the natural conformation of the antigen may be essential for the induction of neutralizing antibody. High titers of antibodies capable of complement-mediated cytolysis (ACC) were induced by gp110 + SAF-M, whereas minimal ACC antibodies were induced by gp140 + FA. In spite of high titers of antibodies by ELISA, neither gp110 + SAF-M nor gp140 + FA vaccines induced detectable levels of antibody capable of antibody dependent cell-mediated cytolysis (ADCC). Detectable amounts of MHC class I-restricted, CD8+ cytotoxic T lymphocytes (CTLs) were not induced in immunized monkeys before challenge. After challenge and infection, antibody responses to glycoprotein (detected by ELISA and ACC) as well as glycoprotein-specific CTLs were induced in gp140 + FA vaccinates at levels higher than in nonimmunized control animals, indicating a priming effect by gp140 + FA immunization. No priming effect for ADCC antibody induction was observed in monkeys vaccinated with either gp110 + SAF-M or gp140 + FA. Rhesus monkey groups immunized with two different SIV envelope vaccines differed regarding potentially protective humoral and cell-mediated immune responses. The physical state of the immunogens, the type of adjuvant used, and/or the immunization protocol apparently affected these responses in both a qualitative and quantitative manner.

CT Check Tags: Animal; Human; Support, U.S. Gov't, P.H.S.

Acetylmuramyl-Alanyl-Isoglutamine: AA, analogs & derivatives

Acetylmuramyl-Alanyl-Isoglutamine: AD, administration & dosage

Antibodies, Viral: BI, biosynthesis

*AIDS Vaccines: IM, immunology

Cells, Cultured

Disease Models, Animal

Enzyme-Linked Immunosorbent Assay

Freund's Adjuvant: IM, immunology

IgG: IM, immunology

Macaca mulatta

Neutralization Tests

Polysorbates: AD, administration & dosage

Retroviridae Proteins: IM, immunology

*Simian Acquired Immunodeficiency Syndrome: IM, immunology

Simian Acquired Immunodeficiency Syndrome: PC, prevention & control

Squalene: AA, analogs & derivatives

Squalene: AD, administration & dosage

T-Lymphocytes, Cytotoxic: IM, immunology

Vaccines, Synthetic: IM, immunology

Viral Envelope Proteins: IM, immunology

RN 111-02-4 (Squalene); **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine)**; 9007-81-2 (Freund's Adjuvant)

WS-B27-2).

CY GERMANY: Germany, Federal Republic of
 DT (CLINICAL TRIAL)
 (CLINICAL TRIAL, PHASE I)
 Abstract
 (RANDOMIZED CONTROLLED TRIAL)

FS ICA9
 LA English
 EM 199311
 AB A phase 1 randomized double-blind study was performed to determine safety and immunogenicity in HIV-seronegative adults of three injections (at day 0 and months 1 and 6) of a vaccine composed of 25 micrograms of recombinant HIV gp 120 (SF-2) antigen combined with MF-59 emulsion containing a muramyl tripeptide (MTP-PE) in a dose escalation format. Forty-two healthy HIV-seronegative adults, with normal laboratory studies were vaccinated. Each vaccine contained MF59 emulsion and each subject received MTP-PE (micrograms per injection) dosing as follows: Group 1 (0/0/0); Group (1/1/1); Group 2 (10/10/10); Group 4 (50/50/50); Group 5 (10/0/0); Group 6 (100/0/0). Two subjects in each group were randomized to receive placebo-antigen while 6 received gp 120. All subjects, except one, received all three immunization. Injections were, in general, well tolerated. ELISA antibodies directed to gp 120 developed in the expected number of subjects. All subjects developing ELISA antibodies also developed neutralizing titers to SF-2 comparable to titers observed in naturally infected subjects. Virus neutralizing to a heterologous strain (MN) has also been observed. Durability of antibody responses has been documented 6 months following the third immunization in the first three groups. Lymphocyte proliferation data has been documented in subjects developing gp120 antibody and has also demonstrated durability over the study period.

CT Check Tags: Human
 *Acetylmuramyl-Alanyl-Isoglutamine: AA, analogs & derivatives
 Acetylmuramyl-Alanyl-Isoglutamine: IM, immunology
 *Adjuvants, Immunologic
 Adult
 *AIDS Vaccines
 AIDS Vaccines: AD, administration & dosage
 AIDS Vaccines: IM, immunology
 Dose-Response Relationship, Immunologic
 Double-Blind Method
 Emulsions
 HIV Antibodies: BI, biosynthesis
 HIV Envelope Protein gp120: AD, administration & dosage
 *HIV Envelope Protein gp120: IM, immunology
 *HIV-1: IM, immunology
 Neutralization Tests
 *Phosphatidylethanolamines: IM, immunology
 Recombinant Proteins: AD, administration & dosage
 Recombinant Proteins: IM, immunology
 Safety
 Vaccines, Synthetic: AD, administration & dosage
 Vaccines, Synthetic: IM, immunology

RN 53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine); 83461-56-7
 (CGP 19835 A)

CN 0 (Adjuvants, Immunologic); 0 (AIDS Vaccines); 0 (Emulsions); 0 (HIV Antibodies); 0 (HIV Envelope Protein gp120); 0 (Phosphatidylethanolamines); 0 (Recombinant Proteins); 0 (Vaccines,

Synthetic)

L76 ANSWER 13 OF 38 AIDSLINE
AN 1993:12524 AIDSLINE
DN ICA9-93335769
TI A phase I HIV-1 vaccine trial in asymptomatic HIV-infected individuals using Env 2-3 in MF-59 with or without MTP-PE. NIAID AVEG.
AU Corey L; McElrath J; Keefer M; Paxton W; Sposto R; Chernoff D
CS Univ of Washington, Seattle.
SO Int Conf AIDS, (1993). Vol. 9, No. 1, pp. 494 (Abstract No. PO-B28-2152).
CY GERMANY: Germany, Federal Republic of
DT (CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE I)
Abstract
(RANDOMIZED CONTROLLED TRIAL)
FS ICA9
LA English
EM 199311
AB OBJECTIVES: To evaluate the safety and virologic responses in asymptomatic HIV-infected individuals following immunization with a gp120 subunit HIV-1SF-2 vaccine and MTP-PE adjuvant in a randomized, blinded, controlled trial. METHODS: Asymptomatic HIV-1-infected persons lacking plasma viremia with CD4 counts > 600 cells/ul (Group A, N = 30) or 400-550 cells/ul (Group B, N = 15) were immunized with either Env 2-3 (30 micrograms) in MF59 100 micrograms MTG-PE or MF59 100 micrograms MTP-PE at months 0, 1, and 4. Immunizations at months 7 and 10 are in progress. Serial measurements of CD4 cell count, quantitative PBMC viral culture, plasma virus culture, PBMC DNA PCR, and plasma RNA PCR were made. RESULTS: The vaccine was associated with both local pain and systemic symptoms in 82% and 40% of recipients, respectively. All symptoms resolved within 48-72 hours, and no volunteer refused further vaccination as a result of these symptoms. To date, no statistically significant differences in CD4 cell count and quantitative PBMC culture have been seen in the treatment vs control groups. Analysis of the frequency of plasma viremia, quantitative PBMC DNA PCR, and quantitative plasma RNA PCR data are in progress; preliminary analysis suggest a trend in one of the vaccine groups. CONCLUSIONS: The Env 2-3 vaccine in MF59 MTP-PE was safe, and was not associated with a discernable increase in HIV replication. At present, no detectable alterations in CD4 cell counts or in quantitative PBMC viral culture have been found between vaccine-treated or untreated subjects. However, complete analysis of the quantitative PCR data are pending.
CT Check Tags: Human
Acetylmuramyl-Alanyl-Isoglutamine: AA, analogs & derivatives
Adjuvants, Immunologic
*AIDS Vaccines: TU, therapeutic use
Double-Blind Method
DNA, Viral: BL, blood
*HIV Envelope Protein gp120: IM, immunology
HIV Infections: BL, blood
HIV Infections: MI, microbiology
*HIV Infections: TH, therapy
*HIV-1: IM, immunology
HIV-1: IP, isolation & purification
Phosphatidylethanolamines

Polymerase Chain Reaction
Provirus: IP, isolation & purification
Recombinant Proteins: IM, immunology
RNA, Viral: BL, blood
Safety
Vaccines, Synthetic: IM, immunology
Viremia: BL, blood
Viremia: MI, microbiology
*Viremia: TH, therapy

RN **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine);** 83461-56-7
(CGP 19835 A)

CN 0 (Adjuvants, Immunologic); 0 (AIDS Vaccines); 0 (DNA, Viral); 0
(HIV Envelope Protein gp120); 0 (Phosphatidylethanolamines); 0
(Recombinant Proteins); 0 (RNA, Viral); 0 (Vaccines, Synthetic)

L76 ANSWER 14 OF 38 AIDSLINE
AN 1993:11206 AIDSLINE
DN ICA9-93334177
TI Phase I trial of native HIV-1SF-2 rgp120 candidate vaccine. NIAID
AIDS Vaccine Clinical Trials Network.
AU Graham B; Keefer M; McElrath J; Matthews T; Schwartz D; Gorse G;
Sposto R; Chernoff D
CS Vanderbilt Univ., Nashville, TN.
SO Int Conf AIDS, (1993). Vol. 9, No. 1, pp. 250 (Abstract No.
PO-A29-0692).
CY GERMANY: Germany, Federal Republic of
DT (CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE I)
Abstract
(RANDOMIZED CONTROLLED TRIAL)

FS ICA9
LA English
EM 199311

AB OBJECTIVES: To evaluate the safety and immunogenicity of rgp120 from
HIV-1SF-2 in MF59 emulsion formulated with or without MTP-PE
(Biocine, Emeryville, CA). METHODS: Healthy, HIV-seronegative, low
risk adult volunteers were immunized at 0, 1, and 6 months with 15
micrograms or 50 micrograms of rgp120 in MF59 with or without 50
micrograms of MTP-PE. Another group of healthy adult women received
5 monthly injections of MF59 alone or 50 micrograms rgp120 in MF59.
The studies were randomized and double-blind. Clinical responses and
laboratory toxicities were monitored and immune responses were
analyzed. RESULTS: 12/48 volunteers had significant erythema or
induration at the site of vaccination; 9/12 received MTP-PE. All 4
with significant local pain and tenderness received MTP-PE as did
7/9 with significant fever, malaise, or headache. Serologic data 1
month after the third dose is presented below as mean O.D. or titer
among responders and fraction of responders. V3 = peptide ELISA; NT
= neutralization; FI = fusion inhibition. TABULAR DATA, SEE ABSTRACT
VOLUME. CONCLUSIONS: The Biocine HIV-1SF-2 native rgp120 product is
safe and immunogenic. MTP-PE increases local and systemic side
effects, and has no significant adjuvant effect for humoral
responses beyond that afforded by MF59. Three injections of 50
micrograms rgp120 induced type-specific functional antibody
responses in 19/21 vaccinees tested to date.

CT Check Tags: Comparative Study; Female; Human
**Acetylmuramyl-Alanyl-Isoglutamine: AA, analogs &
derivatives**
Acetylmuramyl-Alanyl-Isoglutamine: AD, administration &

currently being examined in animal and human trials for their suitability as adjuvants in potential vaccines against acquired immunodeficiency syndrome (AIDS). It may prove to be beneficial to select adjuvants that do not induce NF-kappa B activation and particularly if the vaccines are to be aimed at seropositive individuals. We have examined a battery of synthetic immunostimulants of the muramyl peptide family for their ability to activate NF-kappa B in human and mouse cell lines. In this report, we demonstrate selective activation of NF-kappa B in different cell lines and by different muramyl peptides possessing immunostimulatory activities. The mechanism of such activation is apparently via production of reactive oxygen intermediates (ROI) since pretreatment of cells with antioxidants blocked subsequent activation of NF-kappa B. However, among all the molecules tested only one lipophilic, non-pyrogenic adjuvant active muramyl peptide showed a complete lack of NF-kappa B activation in all cell lines tested. This molecule could well become the adjuvant of choice in future AIDS vaccines.

CT Check Tags: Animal; Human; In Vitro

Acetylmuramyl-Alanyl-Isoglutamine: CH, chemistry

***Acetylmuramyl-Alanyl-Isoglutamine: IM, immunology**

*Acquired Immunodeficiency Syndrome: TH, therapy

*Adjuvants, Immunologic

Antioxidants: PD, pharmacology

Base Sequence

Cell Line

Gene Expression

Interleukin-8: GE, genetics

Mice

Molecular Sequence Data

*NF-kappa B: ME, metabolism

Oligodeoxyribonucleotides: CH, chemistry

Reactive Oxygen Species: ME, metabolism

Structure-Activity Relationship

RN **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine)**

CN 0 (Adjuvants, Immunologic); 0 (Antioxidants); 0 (Interleukin-8); 0 (NF-kappa B); 0 (Oligodeoxyribonucleotides); 0 (Reactive Oxygen Species)

L76 ANSWER 20 OF 38 AIDSLINE

AN 1992:11415 AIDSLINE

DN ICA8-92400540

TI Purified inactivated SIV vaccine: comparison of adjuvants.

AU Vaslin B; Le Grand R; Vogt G; Roques P; Stoeckel P; Salk J; Dormont D

CS CRSSA/CEA, Fontenay aux Roses, France.

SO Int Conf AIDS, (1992). Vol. 8, No. 2, pp. A42 (Abstract No. PoA 2239).

CY Netherlands

DT Abstract

FS ICA8

LA English

EM 199212

AB OBJECTIVE: To compare the effects of two adjuvant formulations of purified and inactivated SIV delta, in the Rhesus Macaque, in terms of specific humoral and cellular immune responses, and protection. MATERIAL AND METHODS: The immunogen, delta strain of SIV, was produced on Hut 78 cells, banded onto consecutive sucrose gradients, and inactivated with beta-propiolactone and gamma-irradiation. One group of 5 animals (A) received 3 IM doses of 100 micrograms

immunogen in an oil-in-water emulsion using RIBI adjuvant containing mycobacterial cell wall skeleton and monophospholipid (CWS/MPL). A second group of 5 monkeys (B) received 3 IM doses of 100 micrograms immunogen in a water-in-oil emulsion using IFA containing CWS/MPL, followed by 1 IM dose of 100 micrograms immunogen in IFA. Animals were vaccinated on days 0, 56 and 194. Specific ELISA, Western Blot, and lymphocyte proliferative responses to SIV delta were performed every two weeks. Neutralizing antibodies titers, blood cell counts, CD4, CD8 cell counts, blood chemistry, and anti-cell antibodies were also monitored. Three months after the last dose animals were challenged IV with 10 to 100 AID50 of cell-free SIVmac251 produced on rhesus PBLs, along with a non vaccinated control group. RESULTS: In group A, anti SIV antibody titers transiently reached 4 to 5 log10 after 2-3 injections but no specific proliferative responses were detectable. Group B animals showed high (5-6 log10) and more stable titers after 1-2 injections; high proliferative responses were detected in this group. After the 3rd injection, proliferative responses were seen as early as 48 hours after initiating in vitro immunogen stimulation, with an optimum at 72 hours. Group B, but not Group A, animals exhibited neutralizing antibodies on the day of challenge. Monkeys in both groups developed anti-human-cell antibodies. Autoimmune-like symptoms were observed in 2 animals in group B. The outcome of challenge is under investigation. CONCLUSION: CWS/MPL(RIBI adjuvant) induced immunologic responses comparable to those produced by alum and by MDP-containing adjuvants when used with a similar immunogen, as previously reported by other investigators. The CWS/MPL+IFA adjuvant produced stronger immunological responses (both humoral and cell-mediated); however, autoimmune-like symptoms were observed in 2/5 animals. Studies with other adjuvants and combinations of adjuvants are underway for the purpose of identifying those that produce protective immunologic responses without inducing undesirable side effects.

CT Check Tags: Animal; Comparative Study

Acetylmuramyl-Alanyl-Isoglutamine: IM, immunology

*Adjuvants, Immunologic

*Cord Factors: IM, immunology

Freund's Adjuvant: IM, immunology

Immunity, Cellular

*Lipid A: AA, analogs & derivatives

Lipid A: IM, immunology

*Macaca mulatta: IM, immunology

Simian Acquired Immunodeficiency Syndrome: PC, prevention & control

*SIV: IM, immunology

Vaccines, Inactivated: IM, immunology

*Viral Vaccines

Viral Vaccines: IM, immunology

RN **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine);** 9007-81-2
(Freund's Adjuvant)

CN 0 (Adjuvants, Immunologic); 0 (Cord Factors); 0 (Lipid A); 0 (Ribi adjuvant); 0 (Vaccines, Inactivated); 0 (Viral Vaccines)

L76 ANSWER 21 OF 38 AIDSLINE

AN 1992:11199 AIDSLINE

DN ICA8-92400280

TI Protection of rhesus macaques from cell-free and cell-associated SIV challenge, by vaccination with SIV iscoms or MDP adjuvanted inactivated SIV.

AU De Vries P; Heeney J; Morein B; Osterhaus A D

CS Laboratory of Immunobiology, RIVM, Bilthoven, The Netherlands.

SO Int Conf AIDS, (1992). Vol. 8, No. 1, pp. We52 (Abstract No. WeD 1042).

CY Netherlands

DT Abstract

FS ICA8

LA English

EM 199212

AB OBJECTIVES: Comparison of protection afforded by iscome and MDP adjuvanted whole inactivated virus in a SIV-macaque model. METHODS: Eight macaques (*Macaca mulatta*) were vaccinated four times with an SIV iscom vaccine, eight with an MDP adjuvanted whole inactivated SIV vaccine, four with a measles virus (MV) iscom vaccine and four with an MDP adjuvanted inactivated whole MV vaccine. They were all challenged with either 10MID50 of the homologous cell-free SIVmac251 (32H) propagated in C8166 cells or with 10MID50 of SIV-infected PBMC directly taken from a monkey suffering from AIDS after infection with the SIVmac251 (32H) strain. RESULTS: All the monkeys vaccinated with SIV-MDP and SIV-iscom and challenged with cell-free SIVmac251 (32H) were protected from developing SIV viraemia, whereas all the MV-MDP and MV-iscom vaccinated monkeys developed SIV-viraemia within four weeks after cell-free challenge. Also all the MV-MDP and MV-iscom vaccinated animals challenged with SIV infected PBMC developed viraemia within 2 weeks. Two out of four SIV-MDP vaccinated and two out of four SIV-iscom vaccinated monkeys challenged with SIV infected PBMC were protected from SIV viraemia. The data were confirmed by serological tests and PCR analyses. CONCLUSION: This is the first demonstration that vaccination can protect macaques from challenge with SIV infected PBMC. This protection should be attributed to immunization with SIV-specific antigens since the challenge was carried out directly with SIV infected PBMC of the homologous species.

CT Check Tags: Animal; Comparative Study

Acetylmuramyl-Alanyl-Isoglutamine: AD, administration & dosage

Macaca mulatta

*Simian Acquired Immunodeficiency Syndrome: PC, prevention & control

*SIV: IM, immunology

Vaccines, Inactivated: AD, administration & dosage

*Viral Vaccines: AD, administration & dosage

Viremia: PC, prevention & control

RN **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine)**

CN 0 (Vaccines, Inactivated); 0 (Viral Vaccines)

L76 ANSWER 22 OF 38 AIDSLINE

AN 1992:11016 AIDSLINE

DN ICA8-92400075

TI Phase 1 dose escalation MTP-PE study of an HIV-1 gp120 vaccine in sero-negative adults.

AU Kahn J; Chernoff D; Sinangil F; Murcar N; Wynne D; Coleman R; Haigwood N; Steimer K; Dekker C

CS AIDS Division, San Francisco General Hospital, University of California.

SO Int Conf AIDS, (1992). Vol. 8, No. 1, pp. Mo9 (Abstract No. MoB 0025).

CY Netherlands

DT Abstract

FS ICA8

LA English

EM 199212

AB OBJECTIVES: We conducted a phase 1 randomized double-blind study to determine safety and immunogenicity in HIV-seronegative adults of three injections of a vaccine composed of 25 micrograms of recombinant HIV gp 120 antigen combined with MF 59 emulsion containing a muramyl tripeptide covalently linked with dipalmitoyl phosphatidylethanolamine (MTP-PE) at different concentrations. Specifically we examined the ability of the candidate vaccine to elicit ELISA and neutralizing antibodies against HIV, the immunologic stimulatory properties of the adjuvant as well as the effects of the vaccine candidate. METHODS: The vaccine antigen is recombinant gp 120 from the SF2 strain of HIV-1, expressed in Chinese hamster ovary cells. The gp 120 vaccine is fully glycosylated and exhibits CD4 binding activity. Forty-two healthy HIV-seronegative adult men and women, with normal laboratory studies and without identifiable high-risk behavior for HIV infection were vaccinated. Vaccination occurred at day 0, 1 month and at 6 months. Vaccinees will be followed for 6 months after last injection. Subjects were entered into the study according to the following design: TABULAR DATA, SEE ABSTRACT VOLUME. Each vaccine contained MF59 emulsion and each subject in the different groups received MTP-PE dosing as scheduled above. Two subjects in each group were randomized to receive placebo-antigen while 6 received gp 120 at 25 micrograms dose. RESULTS: To date, subjects tolerated vaccination well. Symptoms reported include mild muscle aches, headache, low grade fevers. All symptoms were graded as mild. One subject in group 3 had a transient increase in liver function studies and bilirubin that resolved without interruption of the vaccine administration. One subject in Group 3 left the study. Five subjects in groups 1, 2 and 3, after only 2 immunizations, have developed HIV neutralizing antibodies. No subject has yet received a third immunization, and not all individuals in Groups 4 and 6 have received a second immunization. CONCLUSIONS: Initial information suggests that this candidate HIV vaccine is well tolerated. The relative toxicities of the candidate vaccine, the development of neutralizing antibodies and the immunologic effects of vaccination will be presented. Ultimate study conclusions will be based upon the complete and final data set.

CT Check Tags: Human

Acetylmuramyl-Alanyl-Isoglutamine: AA, analogs & derivatives

Adult

*AIDS Vaccines

Double-Blind Method

Enzyme-Linked Immunosorbent Assay

*HIV Antibodies: BI, biosynthesis

HIV Antibodies: IM, immunology

HIV Envelope Protein gp120: AD, administration & dosage

*HIV Envelope Protein gp120: IM, immunology

*HIV Seropositivity

*HIV-1: IM, immunology

Immunization, Secondary

Neutralization Tests

Phosphatidylethanolamines

Recombinant Proteins: AD, administration & dosage

Recombinant Proteins: IM, immunology

Safety

*Vaccination

*Vaccines, Synthetic

RN 53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine); 83461-56-7

(CGP 19835 A)
 CN 0 (AIDS Vaccines); 0 (HIV Antibodies); 0 (HIV Envelope Protein gp120); 0 (Phosphatidylethanolamines); 0 (Recombinant Proteins); 0 (Vaccines, Synthetic)

L76 ANSWER 23 OF 38 AIDSLINE
 AN 1992:11009 AIDSLINE
 DN ICA8-92400068
 TI Vaccine protection from SIV infected cell challenge is MHC class I related.
 AU Heeney J; Bontrop R; Van Els C; De Vries P; Jonker M; Osterhaus A
 CS Dept. of Chronic and Infectious Diseases, ITRI-TNO, Rijswijk, The Netherlands.
 SO Int Conf AIDS, (1992). Vol. 8, No. 1, pp. Mo7 (Abstract No. MoA 0018).
 CY Netherlands
 DT Abstract
 FS ICA8
 LA English
 EM 199212
 AB OBJECTIVE: To determine if vaccine protection against infected cells is related to the MHC type of donor and recipient. METHODS: Twenty four MHC typed Macaca mulatta vaccinated with either formalin inactivated whole SIV adjuvanted with MDP (n = 8) or in ISCOM (n = 8) preparations. Controls included measles virus (MV) MDP (n = 4) or ISCOM (n = 4) controls. Half of the group was homologously challenged with 10 MID50 of cell-free SIVmac32H. The other half of the group was challenged with 10 MID50 of peripheral blood mononuclear (PBMCs) from an SIVmac32H infected macaque with AIDS. RESULTS: All SIV vaccinated animals challenged with homologous cell-free SIVmac32H were protected. Antibody responses against the cell line used to produce the vaccine did not correlate with protection (Osterhaus et al., Nature 1991; 355, 685). Of the animals challenged with an equivalent infectious dose of PBMCs from an SIV infected macaque only half were protected. Animals protected from the cell associated challenge shared a particular MHC class I allele with the donor of the infected cells. CONCLUSION: These results suggest that vaccine protection against cells infected with SIV (or HIV) may recognise antigen in the context of an MHC molecule which is shared between the donor and vaccinated recipient, facilitating a protective cell mediated immune response.
 CT Check Tags: Animal; Comparative Study
 Acetylmuramyl-Alanyl-Isoglutamine: IM, immunology
 Adjuvants, Immunologic
 *Histocompatibility Antigens Class I: PH, physiology
 ISCOMs: IM, immunology
 Leukocytes, Mononuclear: IM, immunology
 Leukocytes, Mononuclear: MI, microbiology
 Leukocytes, Mononuclear: TR, transplantation
 *Macaca mulatta: IM, immunology
 Measles Vaccine
 *Simian Acquired Immunodeficiency Syndrome: PC, prevention & control
 *SIV: IM, immunology
 Vaccination
 *Viral Vaccines: IM, immunology
 RN **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine)**
 CN 0 (Adjuvants, Immunologic); 0 (Histocompatibility Antigens Class I); 0 (ISCOMs); 0 (Measles Vaccine); 0 (Viral Vaccines)

AB Rhesus macaques (*Macaca mulatta*) immunized with an inactivated whole SIVmac vaccine and muramyl dipeptide (MDP), incomplete Freund's adjuvant (IFA), or aqueous suspension were challenged intravenously with 0.1 TCID₅₀ of cell-free SIVmac. Whereas virus was readily recovered from the peripheral blood lymphocytes of 10 of 10 nonvaccinated controls following this challenge dose, virus was not recovered from the three animals that received the vaccine with MDP nor from one of two animals that received the vaccine with IFA and one of three animals that received the aqueous vaccine. The animals that were protected against challenge were those that had detectable SIV antibody response to the envelop, both the outer glycoprotein (gp120) and the truncated transmembrane glycoprotein (gp31). Protected monkeys tended to have higher titers of syncytial inhibition antibody prior to challenge. An anamnestic response after challenge was observed only in the vaccinated monkeys that became infected. Vaccinated animals that became challenge-infected tended to live longer than infected controls. These results confirm those at two other primate centers and indicate that killed whole SIV vaccines can protect against low challenge doses of SIV and prevent early death in those monkeys that do become infected. The mechanism of this protection remains undetermined. This finding adds optimism to the possibility of an eventual AIDS vaccine.

CT Check Tags: Animal; Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.

Acetylmuramyl-Alanyl-Isoglutamine: IM, immunology
Antibodies, Viral: BI, biosynthesis
Antigens, Viral: IM, immunology
Base Sequence
Cell Line
Freund's Adjuvant: IM, immunology
Giant Cells: CY, cytology
Immunoblotting
Immunoenzyme Techniques
Immunologic Memory
Macaca mulatta
Molecular Sequence Data
*Simian Acquired Immunodeficiency Syndrome: PC, prevention & control
*SIV: IM, immunology
Vaccination
Vaccines, Inactivated: IM, immunology
Viral Envelope Proteins: IM, immunology
*Viral Vaccines: IM, immunology

RN **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine); 9007-81-2**
(Freund's Adjuvant)

CN 0 (Antibodies, Viral); 0 (Antigens, Viral); 0 (Vaccines, Inactivated); 0 (Viral Envelope Proteins); 0 (Viral Vaccines)

L76 ANSWER 28 OF 38 AIDSLINE
AN 1991:4760 AIDSLINE
DN ASM90-905018
TI Protection for macaques against SIVmac challenge using an inactivated whole virus vaccine.
AU Carlson J R; McGraw T P; Keddie E; Jennings M B; Vowels B; Gardner M B
CS Med. Pathology, Univ. California, Davis.
SO Abstr Annu Meet Am Soc Microbiol, (1990). Vol. 90, pp. 338 (Abstract No. T-13).
ISSN: 0094-8519.
CY United States

DT Abstract
 FS ASM90
 LA English
 EM 199107
 AB Rhesus monkeys were immunized by multiple inoculations with purified, inactivated SIVmac (ISIV). Experimental groups included animals that received the SIVmac immunogen in muramyl dipeptide, incomplete Freund's adjuvant, or in aqueous suspension. ISIV immunized animals developed anti-SIV antibodies and positive, SIV specific, T cell proliferation responsiveness. Monkeys were challenged with infectious cell-free SIVmac by an intramuscular inoculation. SIV isolation from peripheral blood was used to evaluate infection following the challenge. None of the 3 animals that received ISIV/MDP became viremic after challenge. One of 2 animals that received ISIV/IFA, 2/3 that received Aq ISIV and 4/4 controls became viremic. These results confirm two recent reports that vaccination with inactivated whole virus can protect macaques against challenge with live SIV.

CT Check Tags: Animal
Acetylmuramyl-Alanyl-Isoglutamine
 Antibodies, Viral: IM, immunology
 Freund's Adjuvant
 Lymphocyte Transformation
 Macaca mulatta
 *Simian Acquired Immunodeficiency Syndrome: PC, prevention & control
 *SIV: IM, immunology
 SIV: IP, isolation & purification
 T-Lymphocytes: IM, immunology
 Vaccines, Inactivated
 *Viral Vaccines

RN **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine)**; 9007-81-2 (Freund's Adjuvant)

CN 0 (Antibodies, Viral); 0 (Vaccines, Inactivated); 0 (Viral Vaccines)

L76 ANSWER 29 OF 38 AIDSLINE
 AN 1991:4709 AIDSLINE
 DN PRIM8-900036
 TI Protection of rhesus macaques from infection with SIVMAC using a formalin inactivated whole virus preparation.

AU Cranage M P; Cook N; Thompson A; Greenaway P J; Baskerville A
 CS Public Health Laboratory Service Centre for Applied Microbiology and Research, Porton Down, Salisbury SP4 0JG, United Kingdom.
 SO Symp Nonhuman Primate Models AIDS, (1990). Vol. 8, pp. 52 (Abstract No. 36).

CY United States
 DT Abstract
 FS PRIM8
 LA English
 EM 199107
 AB Eight rhesus macaques were inoculated with formalin inactivated SIVMAC251 (32H isolate) prepared from cell free supernatant of infected C8166 cells by gel filtration chromatography. Each animal received a total of four intramuscular inoculations of 500 mug administered in threonyl muramyl dipeptide adjuvant (kindly provided by Syntex Corporation). Four animals received a primary inoculation, two boosts at monthly intervals and a final boost two months later and were then challenged intravenously, together with two control animals, two weeks later with 10 MID50 of homologous virus. Virus was isolated from control animals at 12, 27, 40 and 55 days (to

date) post challenge, whereas no virus was recovered from the vaccinated group. These results were confirmed by PCR analysis of DNA from monkey PBL's (personal communication - P. Kitchin, NIBSC). A further four animals were given a primary vaccination, two monthly boosts and a final boost four months later and were then challenged two weeks later with 10 MID50 of SIVDELTA670 (kindly provided by Dr Murphey Corb). Data from the heterologous challenge group are not yet available at the time of writing. All vaccinated animals made strong humoral immune responses. Preliminary data on the analysis of the protective immune response will be presented.

CT Check Tags: Animal

Acetylmuramyl-Alanyl-Isoglutamine: IM, immunology

Antibodies, Viral: BI, biosynthesis

Cells, Cultured

Chromatography, Gel

DNA, Viral: AN, analysis

*Formaldehyde: PD, pharmacology

Leukocytes, Mononuclear: MI, microbiology

Macaca mulatta

Polymerase Chain Reaction

*Simian Acquired Immunodeficiency Syndrome: PC, prevention & control

SIV: DE, drug effects

SIV: GE, genetics

*SIV: IM, immunology

Vaccination

Vaccines, Inactivated

*Viral Vaccines

RN 50-00-0 (Formaldehyde); **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine)**

CN 0 (Antibodies, Viral); 0 (DNA, Viral); 0 (Vaccines, Inactivated); 0 (Viral Vaccines)

L76 ANSWER 30 OF 38 AIDSLINE

AN 1991:4706 AIDSLINE

DN PRIM8-900033

TI SIV vaccine protection of rhesus macaques.

AU Carlson J R; McGraw T P; Keddie E; Yee J L; Rosenthal A; Langlois A J; Dickover R; Donovan R; Luciw P A; Jennings M B; et al

CS Departments of Pathology and Internal Medicine, School of Medicine, California Primate Research Center, University of California, Davis.

SO Symp Nonhum Primate Models AIDS, (1990). Vol. 8, pp. 49 (Abstract No. 33).

CY United States

DT Abstract

FS PRIM8

LA English

EM 199107

AB Rhesus macaques (M.mulatta) immunized with an inactivated whole SIVmac vaccine and muramyl dipeptide (MDP) incomplete Freund's adjuvant (IFA) or aqueous suspension were challenged intravenously with 10 animal infectious doses (ID) (0.1 TCID₅₀) of cell free SIVmac. Whereas virus was readily recovered from the PBLs of 10 of 10 non-vaccinated controls following this challenge dose, virus was not recovered from the three animals that received the vaccine with MDP nor from one of two animals that received the vaccine with IFA and one of three animals that received the aqueous vaccine. The animals that were protected against challenge were those that had more detectable SIV antibody response to the envelope, both the outer glycoprotein (gp120) and the truncated transmembrane

FS MED; Priority Journals
LA English
OS MEDLINE 91069612
EM 199103
AB Cultured monocyte-derived macrophages were productively infected with human immunodeficiency virus in vitro. Treatment of these cells shortly after infection and several times thereafter with the free form of MTP-PE had an inhibitory effect on virus production. When the liposomal formulation of MTP-PE was used, higher levels of protection were achieved. The drug was not only effective when added to cells immediately after infection, but it also reduced virus production by cells with an established infection. When the liposomal formulation of MTP-PE was used only one treatment was required to achieve maximal effects. During these studies it was noted that the placebo liposomes had some effect in reducing the reverse transcriptase levels found in the supernatants of infected cells. This reduction could not be explained by direct cytotoxic effect. Both free and liposomal MTP-PE lipid significantly prevented formation of giant cells during the course of infection as well as reduced the cell associated viral antigen.

CT Check Tags: Human; In Vitro
***Acetylmuramyl-Alanyl-Isoglutamine: AA, analogs & derivatives**
Acetylmuramyl-Alanyl-Isoglutamine: AD, administration & dosage
Acetylmuramyl-Alanyl-Isoglutamine: PD, pharmacology
Antiviral Agents
Dose-Response Relationship, Drug
Drug Carriers
*HIV: DE, drug effects
HIV: EN, enzymology
HIV: PH, physiology
Liposomes
Macrophages: DE, drug effects
Macrophages: EN, enzymology
Macrophages: MI, microbiology
Phosphatidylethanolamines: AD, administration & dosage
*Phosphatidylethanolamines: PD, pharmacology
RNA-Directed DNA Polymerase: AI, antagonists & inhibitors
*Virus Replication: DE, drug effects

RN **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine);** 83461-56-7 (CGP 19835 A)

CN EC 2.7.7.49 (RNA-Directed DNA Polymerase); 0 (Antiviral Agents); 0 (Drug Carriers); 0 (Liposomes); 0 (Phosphatidylethanolamines)

L76 ANSWER 33 OF 38 AIDSLINE
AN 1990:16015 AIDSLINE
DN ICA6-40105090
TI Novel muramyl tripeptide (MTP-PE) adjuvant formulations for enhancement of immunity to recombinant HIV-1 gp120 envelope antigens.
AU Van Nest G; Barchfeld G; Haigwood N; Ott G; Wentworth P; Steimer K
CS Chiron Corporation, Emeryville, California, USA.
SO Int Conf AIDS, (1990). Vol. 6, No. 2, pp. 326 (Abstract No. 1050).
CY United States
DT Abstract
FS ICA6
LA English
EM 199012

*Monocytes: MI, microbiology
Tumor Necrosis Factor: BI, biosynthesis
Virus Replication: DE, drug effects
Zidovudine: PD, pharmacology

RN 30516-87-1 (Zidovudine); 4097-22-7 (Dideoxyadenosine);
53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine); 82115-62-6
(Interferon Type II)

CN 0 (monophosphoryl lipid A); 0 (Cord Factors); 0 (Glycolipids); 0
(Interleukin-1); 0 (Lipid A); 0 (Tumor Necrosis Factor)

L76 ANSWER 36 OF 38 AIDSLINE
AN 1990:1882 AIDSLINE
DN MED-90069604
TI A formalin-inactivated whole SIV vaccine confers protection in
macaques.
AU Murphey-Corb M; Martin L N; Davison-Fairburn B; Montelaro R C;
Miller M; West M; Ohkawa S; Baskin G B; Zhang J Y; Putney S D; et al
CS Delta Regional Primate Research Center, Tulane University,
Covington, LA 70434.
SO SCIENCE, (1989). Vol. 246, No. 4935, pp. 1293-7.
Journal code: UJ7. ISSN: 0036-8075.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
FS MED; Priority Journals; Cancer Journals
LA English
OS MEDLINE 90069604
EM 199003
AB A vaccine against human immunodeficiency virus (HIV) would be highly
effective in stopping the acquired immunodeficiency syndrome (AIDS)
epidemic. A comprehensive evaluation of potential vaccine
methodologies can be made by means of the simian model for AIDS,
which takes advantage of the similarities in viral composition and
disease potential between simian immunodeficiency virus (SIV)
infection of rhesus macaques and HIV infection in humans.
Immunization with a formalin-inactivated whole SIV vaccine
potentiated with either alum and the Syntex adjuvant threonyl
muramyl dipeptide (MDP) or MDP alone resulted in the protection of
eight of nine rhesus monkeys challenged with ten animal-infectious
doses of pathogenic virus. These results demonstrate that a whole
virus vaccine is highly effective in inducing immune responses that
can protect against lentivirus infection and AIDS-like disease.

CT Check Tags: Animal
Acetylmuramyl-Alanyl-Isoglutamine: IM, immunology
Adjuvants, Immunologic: AD, administration & dosage
Alum Compounds: AD, administration & dosage
Antibodies, Viral: BI, biosynthesis
Chromatography, High Pressure Liquid
Disease Models, Animal
Formaldehyde
Immunization, Secondary
Leukocyte Count
Lymphocytes: IM, immunology
Lymphocytes: MI, microbiology
Macaca mulatta
*Retroviridae Infections: PC, prevention & control
Retroviridae Proteins: IM, immunology
*SIV: IM, immunology
SIV: IP, isolation & purification
Vaccines, Inactivated: AD, administration & dosage

Vaccines, Inactivated: IM, immunology
 Viral Vaccines: AD, administration & dosage
 *Viral Vaccines: IM, immunology
 Virion: IM, immunology

RN 10043-01-3 (aluminum sulfate); 50-00-0 (Formaldehyde);
53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine); 66112-59-2
 (N-acetylmuramyl-threonyl-isoglutamine)

CN 0 (Adjuvants, Immunologic); 0 (Alum Compounds); 0 (Antibodies,
 Viral); 0 (Retroviridae Proteins); 0 (Vaccines, Inactivated); 0
 (Viral Vaccines)

L76 ANSWER 37 OF 38 AIDSLINE
 AN 1988:5858 AIDSLINE
 DN ICDB-88647963
 TI DEVELOPMENT OF AN ADJUVANT FORMULATION THAT CAN ELICIT PROTECTIVE
 IMMUNITY AGAINST RETROVIRUSES.
 AU Allison A C; Byars N E
 CS Inst. of Biological Sciences, Syntex Res., Palo Alto, CA 94304.
 SO (1987). Vaccines 87. Modern Approaches to New Vaccines: Prevention
 of AIDS and Other Viral, Bacterial, and Parasitic Diseases. Chanock
 RM et al, eds. New York, Cold Spring Harbor Laboratory, p. 56-9,
 1987.
 DT (MEETING PAPER)
 FS ICDB
 LA English
 OS CANCERLIT 88647963
 EM 198812
 AB Traditional virus vaccines have included attenuated live viruses,
 which elicit both humoral and cell-mediated immunity (CMI), and
 inactivated viruses or their components, which elicit circulating
 IgG antibodies in sufficient concentration to protect humans from
 disease. The cloning and expression of the genes for the hepatitis-B
 virus surface (HBsAg) and core (HBcAg) antigens in yeast and
 Escherichia coli, and the licensing by the Food and Drug
 Administration of the former in a vaccine, open up a new chapter in
 the history of immunization. The full promise of this approach
 requires the development of an adjuvant formulation that, with virus
 and other subunit antigens, elicits the production of antibodies of
 protective isotypes, CMI, and memory in both T- and B-lymphocyte
 populations. The development of an adjuvant formulation is reported
 that meets these requirements and appears to be free from
 unacceptable side effects. A nontoxic small molecule that would be
 the equivalent of the mycobacterial cell-wall component of Freund's
 complete adjuvant was identified: the threonyl analog of muramyl
 dipeptide (MDP). A nonionic detergent with unusual
 properties--Pluronic L121 triblock polymer--was formulated. Both the
 MDP analog and Pluronic formulation are required for optimal
 adjuvant activity: the combination is termed Syntex Adjuvant
 Formulation-1 or SAF-1. This formulation does not produce tissue
 damage or elicit an inflammatory reaction at injection sites, and no
 systemic reaction is demonstrable. A variety of viral subunits,
 monoclonal immunoglobulins, and other antigens have, when
 administered im or sc in SAF-1, elicited high titers of antibodies
 and CMI. Examples of the use of SAF-1 to elicit immunity to viruses
 include the development of an efficacious vaccine against feline
 leukemia virus, protection of rhesus monkeys against simian acquired
 immune deficiency syndrome virus (unsuccessful), and evoking high
 titers of antibodies using HBsAg in laboratory animals.
 Collaborative studies have also shown primary and secondary

responses to recombinant HBsAg and HBcAg in SAF-1, comparable to those in Freund's complete adjuvant. (6 Refs)

CT Check Tags: Animal

Acetylmuramyl-Alanyl-Isoglutamine: AA, analogs & derivatives

Acetylmuramyl-Alanyl-Isoglutamine: IM, immunology

Acquired Immunodeficiency Syndrome: IM, immunology

Acquired Immunodeficiency Syndrome: PC, prevention & control

*Adjuvants, Immunologic

Antibody Formation

Cats

HIV: IM, immunology

Leukemia Virus, Feline: IM, immunology

Macaca mulatta

*Retroviridae: IM, immunology

Vaccination

Viral Vaccines: AD, administration & dosage

*Viral Vaccines: IM, immunology

RN **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine)**

CN 0 (Adjuvants, Immunologic); 0 (Viral Vaccines)

L76 ANSWER 38 OF 38 AIDSLINE

AN 1988:5705 AIDSLINE

DN MED-88288096

TI Possible treatment of AIDS patients with live lactobacteria.

AU Tihole F

SO MEDICAL HYPOTHESES, (1988). Vol. 26, No. 1, pp. 85-8.

Journal code: MOM. ISSN: 0306-9877.

CY ENGLAND: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)

FS MED; Priority Journals

LA English

OS MEDLINE 88288096

EM 198811

AB The enhancement of antimicrobial resistance and immunomodulatory action, and the anabolic effect caused by the consumption of live lactobacteria as a dietary adjunct are proposed by the author as sufficient reasons to test lactobacterial preparations in patients with AIDS. The problem of dosage is discussed and a practical solution presented.

CT Check Tags: Human

Acetylmuramyl-Alanyl-Isoglutamine: TU, therapeutic use

Acquired Immunodeficiency Syndrome: IM, immunology

*Acquired Immunodeficiency Syndrome: TH, therapy

Immunity, Natural

*Immunization: MT, methods

*Lactobacillus acidophilus

*Opportunistic Infections: TH, therapy

Phagocyte Bactericidal Dysfunction: TH, therapy

RN **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine)**

=> d his

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L1 FILE 'REGISTRY' ENTERED AT 09:32:03 ON 08 DEC 1998
2 S 74817-61-1 OR 60355-78-4

L2 FILE 'BIOSIS' ENTERED AT 09:32:36 ON 08 DEC 1998
74 S L1 OR MURABUTIDE OR MURAMETIDE
E RETROVIR/BC
L3 0 S E5 AND L2
L4 2 S E4-E8 AND L2

=> fil biosis

FILE 'BIOSIS' ENTERED AT 09:33:42 ON 08 DEC 1998
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FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 18 November 1998 (981118/ED)
CAS REGISTRY NUMBERS (R) LAST ADDED: 18 November 1998 (981118/UP)

=> d all 14

L4 ANSWER 1 OF 2 BIOSIS COPYRIGHT 1998 BIOSIS
AN 97:420005 BIOSIS
DN 99719208
TI Construction of peptide immunogens and novel delivery systems
(liposomes and ISCOMS) against HIV and gag sequences with
murabutide as an immunoadjuvant.
AU Agrawal L; Sabhnani L; Rao D N
CS AIIMS, New Delhi-110029, India
SO 17th International Congress of Biochemistry and Molecular Biology in
conjunction with the Annual Meeting of the American Society for
Biochemistry and Molecular Biology, San Francisco, California, USA,
August 24-29, 1997. FASEB Journal 11 (9). 1997. A983. ISSN:
0892-6638
DT Conference
LA English
PR Biological Abstracts/RRM Vol. 049 Iss. 010 Ref. 171318
ST MEETING ABSTRACT; HUMAN IMMUNODEFICIENCY VIRUS TYPE 1; HIV-1;
LIPOSOMAL DRUG DELIVERY SYSTEM; ISCOMS; T CELL; PND V3;
IMMUNOSTIMULANT-DRUG; CONSTRUCTION; PEPTIDE IMMUNOGEN; HUMAN
IMMUNODEFICIENCY VIRUS VACCINE; PHARMACOLOGY; METHODOLOGY;
BIOCHEMISTRY AND BIOPHYSICS; DRUG DELIVERY METHOD; BLOOD AND
LYMPHATICS; IMMUNE SYSTEM
RN **74817-61-1** (MURABUTIDE)
CC General Biology-Symposia, Transactions and Proceedings of
Conferences, Congresses, Review Annuals 00520
Cytology and Cytochemistry-Animal *02506
Biochemical Studies-Proteins, Peptides and Amino Acids *10064
Biophysics-Molecular Properties and Macromolecules *10506

Biochemical Studies-Carbohydrates 10068
Pathology, General and Miscellaneous-Inflammation and Inflammatory
Disease *12508
Pathology, General and Miscellaneous-Therapy *12512
Cardiovascular System-Heart Pathology *14506
Blood, Blood-Forming Organs and Body Fluids-Lymphatic Tissue and
Reticuloendothelial System *15008
Endocrine System-General *17002
Muscle-Pathology *17506
Nervous System-Pathology *20506
Pharmacology-Endocrine System *22016
Pharmacology-Immunological Processes and Allergy *22018
Toxicology-Pharmacological Toxicology *22504
Medical and Clinical Microbiology-Virology *36006
Chemotherapy-Antiviral Agents *38506
BC Picornaviridae 02619
Retroviridae 02623
Muridae 86375

IT 60355-78-4, Murametide 60355-78-4D,
Murametide, homologs 60355-79-5
60355-79-5D, homologs 74817-61-1,
Murabutide 74817-61-1D, Murabutide,
homologs 83869-56-1, GM-CSF
127088-99-7 127179-83-3

L62 ANSWER 15 OF 23 HCAPLUS COPYRIGHT 1998 ACS

AN 1994:407303 HCAPLUS

DN 121:7303

TI Muramyl dipeptide derivative in adjuvant not inducing response to autoantigenic determinants

IN Chedid, Louis; Audibert, Francoise; Lefrancier, Pierre

PA **Vacsyn France SA, Fr.**

SO Fr. Demande, 14 pp.

CODEN: FRXXBL

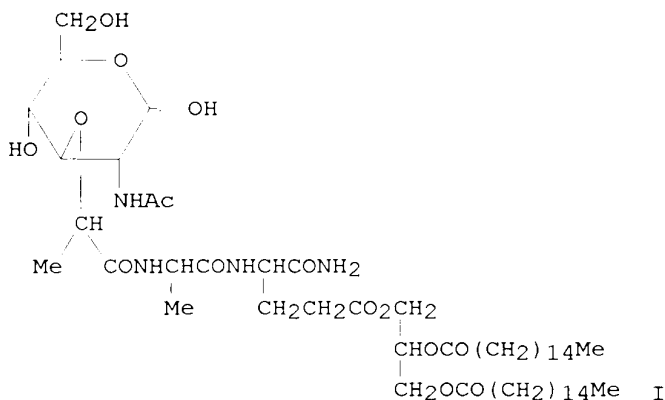
DT Patent

LA French

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	----	-----	-----	-----
PI	FR 2692148	A1	19931217	FR 92-7126	19920612
	FR 2692148	B3	19940819		

GI



AB An adjuvant is disclosed for humoral or cellular immune response or both but without induction of an autoimmune condition from a response to autoantigenic determinants. The adjuvant contains N-acetylmuramyl-D-alanyl-D-[.gamma.-(sn-dipalmitoyl)glycerol]isoglutamine (I). The adjuvant is useful for vaccine compns. which may contain autoantigens, eg. an **AIDS** virus vaccine using virus derived from cultures of human cells or cell lines derived therefrom.

IT **127088-99-7**

RL: BIOL (Biological study)

(adjuvant contg., for lack of response to autoantigen)

L62 ANSWER 16 OF 23 HCAPLUS COPYRIGHT 1998 ACS

AN 1994:215331 HCAPLUS

DN 120:215331

TI Humoral and cell-mediated immunity adjuvant composition inducing no response to autoantigenic determinants

IN Chedid, Louis; Audibert, Francoise; Lefrancier, Pierre

PA **Vacsyn S.A., Fr.**

SO PCT Int. Appl., 28 pp.

CODEN: PIXXD2

DT **Patent**

LA French

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	----	-----	-----	-----
PI	WO 9325236	A1	19931223	WO 93-FR569	19930614
	W: AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	FR 2692149	A1	19931217	FR 92-7125	19920612
	FR 2692149	B1	19950609		
	AU 9343318	A1	19940104	AU 93-43318	19930614
PRAI	FR 92-7125		19920612		
	WO 93-FR569		19930614		
OS	MARPAT 120:215331				
GI					

AU 9748320 A1 19980312 AU 97-48320 19971211
PRAI US 93-48976 19930416
US 90-589422 19900927
US 93-8092 19930122
WO 94-SE340 19940415
AB Novel peptides are disclose which correspond to epitopes of the **HIV**-1 gp120env protein. These antigenic peptides induce antibody-dependent cellular cytotoxicity (ADCC) against **HIV**, and thus are useful in immunization against **HIV** infection and induction of a heightened immune response to **HIV**. Among 41 synthetic peptides covering the entire sequence of **HIV** gp120, 14 showed an ADCC index value greater than 0.5 at a diln. greater than 1:30, in an amt. effective to induce an immune response in a mammal together with a pharmaceutically acceptable carrier. The vaccine compn. further comprises an adjuvant such as Freund's complete adjuvant, Freund's incomplete adjuvant, muramyl dipeptide, levamisole, isoprinosine, or tuftsin.
IT **53678-77-6**, Muramyl dipeptide
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adjuvant; peptides for use in vaccination and induction of neutralizing antibodies against **human immunodeficiency virus**)
L62 ANSWER 14 OF 23 HCAPLUS COPYRIGHT 1998 ACS
AN 1995:240035 HCAPLUS
DN 122:23868
TI Therapeutic compositions for use in humans, characterized by a combination of a muramyl peptide and a **cytokine**
IN Chedid, Louis; **Bahr, Georges**; Lefrancier, Pierre
PA **Vacsyn S. A., Fr.**
SO PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1
PATENT NO. KIND DATE APPLICATION NO. DATE

PI WO 9421275 A1 19940929 WO 94-FR307 19940321
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, UZ, VN
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
FR 2702659 A1 19940923 FR 93-3230 19930319
FR 2702659 B1 19950825
FR 2703251 A1 19941007 FR 93-3787 19930331
FR 2703251 B3 19950804
AU 9462856 A1 19941011 AU 94-62856 19940321
EP 689449 A1 19960103 EP 94-910445 19940321
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE
JP 08511235 T2 19961126 JP 94-520726 19940321
PRAI FR 93-3230 19930319
FR 93-3787 19930331
WO 94-FR307 19940321
OS MARPAT 122:23868
AB A therapeutic compn. for use in humans comprises a combination of

FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9502416	A1	19950126	WO 94-US7749	19940711
	W: AU, BR, CA, CN, JP, KR, NZ				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 5562909	A	19961008	US 93-90841	19930712
	US 5529777	A	19960625	US 93-147781	19931104
	AU 9473286	A1	19950213	AU 94-73286	19940711
	AU 690567	B2	19980430		
	BR 9407397	A	19961105	BR 94-7397	19940711
	JP 09500132	T2	19970107	JP 94-504650	19940711
	EP 792161	A1	19970903	EP 94-923417	19940711
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
PRAI	US 93-90841		19930712		
	US 93-147781		19931104		
	WO 94-US7749		19940711		
AB	Water-sol. polymers or polymeric hydrogels are used to encapsulate antigen to form vaccines. The antigen is mixed with a polymer soln. to form microparticles, and optionally, the polymer may be crosslinked to form stable microparticles. Preferred polymers are alginate and polyphosphazenes, and mixts. thereof. Microparticles can be administered parenterally or mucosally. Intranasal administration of antigens in a polyphosphazene or alginate microspheres induced a serum IgG response.				
IT	53678-77-6 , Muramyl dipeptide				
	RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (hydrogel-microencapsulated vaccines)				

L62 ANSWER 13 OF 23 HCAPLUS COPYRIGHT 1998 ACS

AN 1995:315804 HCAPLUS

DN 122:89368

TI Peptides for use in vaccination and induction of neutralizing antibodies against **human immunodeficiency** virus

IN Vahlne, Anders; Svennerholm, Bo; Rymo, Lars; Jeansson, Stig; Horal, Peter

PA Syntello Vaccine Development AB, Swed.

SO PCT Int. Appl., 75 pp.

CODEN: PIXXD2

DT **Patent**

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9423746	A1	19941027	WO 94-SE340	19940415
	W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KG, KP, KR, KZ, LK, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, UZ, VN				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2160696	AA	19941027	CA 94-2160696	19940415
	AU 9465153	A1	19941108	AU 94-65153	19940415
	EP 693938	A1	19960131	EP 94-912727	19940415
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 09500096	T2	19970107	JP 94-523055	19940415
	US 5840313	A	19981124	US 95-493235	19950620

W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN

RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

FR 2724845 A1 19960329 FR 94-11460 19940926
 FR 2724845 B1 19970117
 CA 2200993 AA 19960404 CA 95-2200993 19950926
 AU 9535699 A1 19960419 AU 95-35699 19950926
 EP 783319 A1 19970716 EP 95-932794 19950926

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE

JP 10506120 T2 19980616 JP 95-511445 19950926

PRAI FR 94-11460 19940926
 WO 95-FR1239 19950926

OS MARPAT 125:26240

AB The use of non-toxic muramyl peptides, particularly **Murabutide** and **Murametide**, to prep. drugs for inhibiting **HIV** replication in humans, is disclosed. The muramyl peptides are capable of up to 100% inhibition of retroviral replication in primary host monocyte cultures.

IT **9001-92-7, Protease**
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors; muramyl peptide compns. with other agents for inhibiting **HIV** replication)

IT **60355-78-4, Murametide 74817-61-1, Murabutide**
 RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (muramyl peptide compns. for inhibiting **HIV** replication)

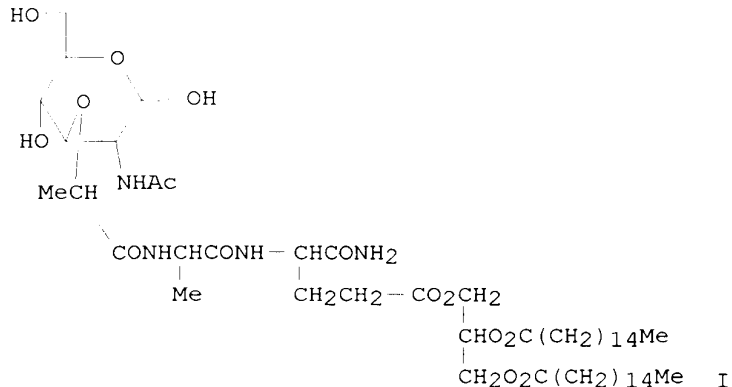
IT **83869-56-1, GM-CSF**
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (muramyl peptide compns. with other agents for inhibiting **HIV** replication)

L62 ANSWER 11 OF 23 HCAPLUS COPYRIGHT 1998 ACS
 AN 1995:899025 HCAPLUS
 DN 123:276025
 TI Use of diesters of muramyl peptides in oral form as immunostimulating agents
 IN Chedid, Louis; Audibert, Francoise; Lefrancier, Pierre
 PA **Vacsyn, S.A., Fr.**
 SO PCT Int. Appl., 35 pp.
 CODEN: PIXXD2
 DT **Patent**
 LA French
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9519777	A2	19950727	WO 95-FR77	19950124
	WO 9519777	A3	19960307		

W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN

RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT,



AB A process is disclosed for the prepn. of a pharmaceutical compn. having a selective immune adjuvant action for humoral response or cell-mediated response, preferably both at once, directed against given antigens, in the absence of any induction of autoimmune disorder linked to a response to autoantigenic determinants. The adjuvant of the invention contains a muramyl peptide deriv. (Markush included), esp. MDP-DD-GDP (I). Absence of induction of autoimmune disorder (allergic encephalomyelitis) in guinea pigs following administration of a water-in oil emulsion of myelin basic protein (autoantigen) with I is described.

IT **127088-99-7**

RL: BIOL (Biological study)
(for adjuvant compn. with no response to autoantigenic determinants)

L62 ANSWER 17 OF 23 HCAPLUS COPYRIGHT 1998 ACS

AN 1993:122811 HCAPLUS

DN 118:122811

TI The control of the antibody isotype response to recombinant **human immunodeficiency** virus gp120 antigen by adjuvants

AU Bomford, R.; Stapleton, M.; Winsor, S.; McKnight, A.; Andronova, T.

CS Wellcome Res. Lab., Beckenham/Kent, BR3 3BS, UK

SO AIDS Res. Hum. Retroviruses (1992), 8(10), 1765-71

CODEN: ARHRE7; ISSN: 0889-2229

DT Journal

LA English

AB Both saponin and muramyl dipeptide (MDP) formulated with a squalane-in-water emulsion of large particle size prepd. with a vortex mixer were superior to Al(OH)₃ as adjuvants for **HIV** gp120 in mice. All the adjuvants induced IgG1 antibody, but saponin elicited the highest titers of IgG2a. The secretion of interleukin-5 (IL-5) and **interferon**-.gamma. (IFN.gamma.) by lymph node cells cultured in vitro with gp120 was studied. All the cultures secreted IL-5, but only those from saponin-immunized mice produced IFN.gamma., suggesting that saponin is capable of activating both the Th1 and Th2 T-cell subsets. The titers of neutralizing antibodies were low with both MDP and saponin, and they occurred in mice which were also pos. for antibodies against a V3 loop peptide. Glucosaminylmuramyl dipeptide (GMDP) which is less

pyrogenic than MDP and a nonpyrogenic analog GMDPA, displayed equiv. adjuvant activity to MDP. The level and isotype compn. of antibodies induced by GMDP in combination with squalane emulsions depended on the dimension of the emulsion particles. With a large (2500 nm) particle size the response was confined to IgG1 in Balb/c mice, but when this was reduced to 150 nm by sonication the antibody response was increased and relatively high levels of IgG2a appeared in some mice.

IT **53678-77-6**, MDP

RL: BIOL (Biological study)

(squalane-in-water emulsion of, antibody isotype response to **human immunodeficiency** virus envelope glycoprotein regulation by)

L62 ANSWER 18 OF 23 HCAPLUS COPYRIGHT 1998 ACS

AN 1992:52347 HCAPLUS

DN 116:52347

TI Synthetic peptide thymosin .alpha.1-N-acetylmuramyl-L-Alanyl-D-isoGlutamyl-L-Lysine

IN Prinzhaus, Gerhard

PA Germany

SO Ger. Offen., 2 pp.

CODEN: GWXXBX

DT **Patent**

LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	----	-----	-----	-----
PI	DE 4010645	A1	19910814	DE 90-4010645	19900327
PRAI	DE 90-4003354	19900210			

AB The title peptide, and also the peptide minus the terminal lysine, stimulates immunoreactivity to thymosin .alpha.1 or thymosin .alpha.1 homologous regions of other proteins. It can be used in treatment of autoimmune disease and **AIDS** (no data).

IT **53678-77-6D**, peptide conjugates

RL: BIOL (Biological study)

(as immunogen for antibodies to thymosin .alpha.1)

L62 ANSWER 19 OF 23 HCAPLUS COPYRIGHT 1998 ACS

AN 1990:434478 HCAPLUS

DN 113:34478

TI Muramyl dipeptide inhibits replication of **human immunodeficiency** virus in vitro

AU Masihi, K. Noel; Lange, Werner; Rohde-Schulz, Beate; Chedid, Louis

CS Robert Koch Inst., West Berlin, Fed. Rep. Ger.

SO AIDS Res. Hum. Retroviruses (1990), 6(3), 393-9

CODEN: ARHRE7; ISSN: 0889-2229

DT Journal

LA English

AB In the search for compds. capable of inducing endogenous prodn. of **colony-stimulating** factor (CSF) and possessing activity against **human immunodeficiency** virus (**HIV**), an immunomodulator, muramyl dipeptide (MDP), was investigated. MDP exhibited an inhibitory activity against **HIV** infection of CD4+ H9 lymphocytes and U937 monocytoid cells. An inhibitor of viral reverse transcriptase, 2', 3'-dideoxyadenosine, produced potent inhibition in cultures which were similarly infected with **HIV**. MDP could partially reduce prodn. in persistently **HIV**-infected KE37/1

RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE
 US 4705756 A 19871110 US 85-734799 19850516
 AU 8659594 A1 19861204 AU 86-59594 19860516
 EP 222891 A1 19870527 EP 86-903840 19860516
 R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE
 JP 63500264 T2 19880128 JP 86-503182 19860516
 US 4814247 A 19890321 US 87-34101 19870316
 US 4900679 A 19900213 US 88-236039 19880823
 PRAI US 85-734799 19850516
 US 83-440540 19830126
 US 83-538783 19831004
 US 85-703120 19850219
 WO 86-US1075 19860516
 US 87-34101 19870316
 AB The effect of an immunomodulator on reaction parameters (e.g. clotting parameters) in a cellular hematol. fluid is an index of the presence of a pathol. condition (e.g. sepsis, premyocardial infarction, cancer, diabetes, **AIDS**). In cancer patients, the blood recalcification time (RT) in the presence of an immunomodulator (Escherichia coli endotoxin) (RTi) was lower than in normal volunteers, whereas RT in the absence of immunomodulator (RTv) was the same in the two groups. The thrombotic index (RTv/RTi) and percent difference of clotting [(RTv-RTi)/RTv .times. 100] were higher in cancer patients than in normal subjects.
 IT **53678-77-6**
 RL: BIOL (Biological study)
 (blood coagulation parameters response to, diagnosis in relation to)

=> d his 164-

(FILE 'REGISTRY' ENTERED AT 09:06:53 ON 08 DEC 1998)

FILE 'HCAPLUS' ENTERED AT 09:07:57 ON 08 DEC 1998

L64 7 S L41 NOT L62

=> d bib abs hitrn tot

L64 ANSWER 1 OF 7 HCAPLUS COPYRIGHT 1998 ACS
 AN 1997:645517 HCAPLUS
 DN 127:314522
 TI Study of the adjuvant activity of new MDP derivatives and purified saponins and their influence on **HIV**-1 replication in vitro
 AU Krivorutchenko, Yuri L.; Andronovskaja, Irina B.; Hinkula, Jorma; Krivoshein, Yuri S.; Ljungdahl-Stahle, Ewa; Pertel, Sergey S.; Grishkovets, Vladimir I.; Zemlyakov, Alexander E.; Wahren, Britta
 CS Department of Microbiology and Virology, Crimean Medical Institute, Simferopol, 333670, Ukraine
 SO Vaccine (1997), 15(12/13), 1479-1486
 CODEN: VACCDE; ISSN: 0264-410X
 PB Elsevier
 DT Journal
 LA English
 AB Muramyl dipeptide (MDP), eight new lipophilic MDP derivs. (MDPs) and three purified saponins were evaluated for their ability to induce immune responses in mice immunized with **HIV**-1 envelope protein rgp160 and for their ability to influence the **HIV**

- 1 replication in vitro. Three of nine new synthetic MDP derivs. (.beta.-butyl-MDP, MTPO-26 and .beta.-cholesteryl-MDP) and one saponin (Taurosid I) have been shown to induce strong humoral immune responses to **HIV**-1 envelope glycoproteins rgp160 and rgp120. Three substances (.beta.-butyl-MDP, MDP-choyl and .beta.-G27-MDP) induced high levels of T-cell stimulation to **HIV**-1 rgp160. .beta.-Butyl-MDP induced the strongest B- and T-cell responses to **HIV**-1 glycoproteins. Two substances (.beta.-butyl-MDP and Taurosid I) did not induce an enhancement of **HIV**-1 replication in vitro and can be considered as promising adjuvants.
- IT **53678-77-6**, Muramyl dipeptide
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adjuvant activity of muramyl dipeptide derivs. and purified saponins and their influence on **HIV**-1 replication in vitro)
- L64 ANSWER 2 OF 7 HCAPLUS COPYRIGHT 1998 ACS
AN 1997:295348 HCAPLUS
DN 126:338421
TI Effects of saponins derived from *Hedera taurica* Carr and modified muramylpeptides on the in vitro reproduction of **human immunodeficiency** virus
AU Krivorutchenko, Yu. L.; Andronovskaya, I. B.; Chirva, V. Ya.; Pertel, S. S.; Grishkovets, V. I.; Zemlyakov, A. Ye.; Kuryanov, V. O.; Krivoshein, Yu. S.
CS Russia
SO Vopr. Virusol. (1997), 42(1), 34-36
CODEN: VVIRAT; ISSN: 0507-4088
PB Meditsina
DT Journal
LA Russian
AB The effects of muramyl dipeptide (MDP), several MDP derivs., and saponins derived from *Hedera taurica* Carr. on the in vitro replication of **HIV**-1 in lymphoblasts were studied. The coeff. of alteration of the rate of **HIV** replication was used to compare effects of these substances on virus replication in Jurkat-tat cells. This coeff. was calcd. as the ratio of concns. of **HIV** p24 in supernatants to the amt. of viable cells. Muramylpeptides boosted **HIV** replication. Only one modified muramylpeptide .alpha.-butyl-MDP and tauroside H2 were not capable of boosting **HIV**-1 antigen prodn.
- IT **53678-77-6**, Muramyl dipeptide
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of *Hedera taurica* saponins and muramylpeptides on **HIV**-1 replication in lymphoblasts)
- L64 ANSWER 3 OF 7 HCAPLUS COPYRIGHT 1998 ACS
AN 1997:23840 HCAPLUS
DN 126:88052
TI Immunogenicity of **HIV**-1LAI gp160 and env peptides in squirrel monkey *Saimiri sciureus* using alumina and experimental adjuvants
AU Perraut, R.; Chouteau, P.; Moog, C.; Bonnemains, B.; Kieny, M. P.
CS Laboratoire d'Immunologie Parasitaire, Institut Pasteur de la Guyane Francaise, Cayenne, Fr. Guiana
SO Clin. Exp. Immunol. (1996), 106(3), 434-441

not correlate with protection. Immunization with a whole inactivated vaccine can protect primates from i.v. challenge with a monkey-cell grown cell-free **human immunodeficiency** virus type 2.

IT **53678-77-6**, Muramyl dipeptide
RL: BAC (Biological activity or effector, except adverse); BIOL
(Biological study)
(whole **HIV-2** vaccines and adjuvants induce antibodies
in cynomolgus monkeys)

L64 ANSWER 7 OF 7 HCAPLUS COPYRIGHT 1998 ACS
AN 1992:39571 HCAPLUS
DN 116:39571
TI Native but not denatured recombinant **human**
immunodeficiency virus type 1 gp120 generates broad-spectrum
neutralizing antibodies in baboons

AU Haigwood, Nancy L.; Nara, Peter L.; Brooks, Eric; Van Nest, Gary A.;
Ott, Gary; Higgins, Ketih W.; Dunlop, Nancy; Scandella, Carl J.;
Eichberg, Jorg W.; Steimer, Kathelyn S.
CS Chiron Corp., Emeryville, CA, 94608-2916, USA
SO J. Virol. (1992), 66(1), 172-82
CODEN: JOVIAM; ISSN: 0022-538X
DT Journal
LA English
AB The protection of individuals from **human**
immunodeficiency virus type 1 (**HIV-1**) infection
with an envelope subunit derived from a single isolate will require
the presentation of conserved epitopes in gp120. The objective here
was to test whether a native recombinant gp120 (rgp120) immunogen
would elicit responses to conserved neutralization epitopes that are
not present in a denatured recombinant gp120 antigen from the same
virus isolate. In a large study of baboons, the authors generated
heterologous neutralizing activity with native, glycosylated
rgp120SF2 but not with denatured, nonglycosylated env 2-3SF2. After
repeated exposure to rgp120SF2 formulated with one of several
adjuvants, virus isolates from the United States, the Caribbean, and
Africa were neutralized. The timing of the immunization regimen and
the choice of adjuvant affected the virus neutralization titers both
quant. and qual. Evidently vaccination with native, glycosylated
rgp120 from a single virus isolate, **HIV-SF2**, may elicit a
protective immune response effective against geog. and sequentially
distinct **HIV-1** isolates.

IT **61136-12-7**
RL: BIOL (Biological study)
(neutralizing antibody formation to native recombinant envelope
glycoprotein of **HIV-SF2** virus in baboons response to)

=> d his 166-

(FILE 'HCAPLUS' ENTERED AT 09:07:57 ON 08 DEC 1998)
SEL HIT RN L64

FILE 'REGISTRY' ENTERED AT 09:11:34 ON 08 DEC 1998
L66 2 S E25-E26
L67 1 S L66 NOT L63

=> d ide can 167

REFERENCE 9: 116:39571

REFERENCE 10: 115:151287

=> d his 168-

(FILE 'AIDSLINE' ENTERED AT 09:12:16 ON 08 DEC 1998)

L68 0 S L43
L69 1 S L44
L70 2 S MURABUTIDE OR MURAMETIDE
L71 38 S ACETYLMURAMYL-ALANYL-ISOGLUTAMINE/CT,CN
L72 1 S N-ACETYLMURAMYL-ALANYLGLUTAMINE-N-BUTYL ESTER/CT,CN
L73 38 S L69-L72
L74 37 S L32
L75 0 S L74 NOT L73
L76 38 S L73,L74

FILE 'EMBASE' ENTERED AT 09:15:23 ON 08 DEC 1998

L77 0 S L43
L78 30 S L44
L79 61 S MURABUTIDE/CT OR MURAMETIDE/CT
L80 61 S L78,L79
L81 0 S L80 AND HIV
L82 0 S L80 AND AIDS
L83 4 S L80 AND IMMUNODEFICIEN?
E HUMAN IMMUNODEFICIEN/CT
E E4+ALL/CT
L84 32362 S E5+NT/CT
E HUMAN IMMUNODEFICIEN/CT
E E87+ALL/CT
L85 68908 S E6+NT/CT
L86 0 S L80 AND L84,L85
L87 1 S L83 AND HUMAN IMMUNODEFICIEN?

=> fil embase

FILE 'EMBASE' ENTERED AT 09:21:05 ON 08 DEC 1998

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FILE COVERS 1974 TO 3 Dec 1998 (19981203/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all 187

L87 ANSWER 1 OF 1 EMBASE COPYRIGHT 1998 ELSEVIER SCI. B.V.
AN 94150769 EMBASE
TI Liposomes, muramyl dipeptide derivatives, and nontoxic lipid a
derivatives as adjuvants for human malaria vaccines.
AU Hui G.S.N.
CS Department of Tropical Medicine, Leahy Hospital, 3675 Kilauea
Avenue, Honolulu, HI 96816, United States
SO AM. J. TROP. MED. HYG., (1994) 50/4 SUPPL. (41-51).
ISSN: 0002-9637 CODEN: AJTHAB
CY United States

Ljungdahl-Stahle E; Pertel S S; Grishkovets V I; Zemlyakov A E; Wahren B
CS Department of Microbiology and Virology, Crimean Medical Institute, Ukraine.
SO VACCINE, (1997). Vol. 15, No. 12-13, pp. 1479-86.
Journal code: X60. ISSN: 0264-410X.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
FS MED; Priority Journals
LA English
OS MEDLINE 97448354
EM 199712
AB Muramyl dipeptide (MDP), eight new lipophilic MDP derivatives (MDPs) and three purified saponins were evaluated for their ability to induce immune responses in mice immunized with HIV-1 envelope protein rgp160 and for their ability to influence the HIV-1 replication in vitro. Three of nine new synthetic MDP derivatives (beta-butyl-MDP, MTPO-26 and beta-cholesteryl-MDP) and one saponin (Taurosud I) have been shown to induce strong humoral immune responses to HIV-1 envelope glycoproteins rgp160 and rgp120. Three substances (beta-butyl-MDP, MDP-cholyl and beta-G27-MDP) induced high levels of T-cell stimulation to HIV-1 rgp160. beta-butyl-MDP induced the strongest B- and T-cell responses to HIV-1 glycoproteins. Two substances (beta-butyl-MDP and Taurosud I) did not induce an enhancement of HIV-1 replication in vitro and can be considered as promising adjuvants.
CT Check Tags: Animal; Female; Male; Support, Non-U.S. Gov't
Acetylmuramyl-Alanyl-Isoglutamine: AA, analogs & derivatives
***Acetylmuramyl-Alanyl-Isoglutamine: PD, pharmacology**
*Adjuvants, Immunologic: PD, pharmacology
*HIV-1: DE, drug effects
HIV-1: PH, physiology
Mice
Mice, Inbred BALB C
*Saponins: PD, pharmacology
*Virus Replication: DE, drug effects
RN **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine)**
CN 0 (Adjuvants, Immunologic); 0 (Saponins)

L76 ANSWER 4 OF 38 AIDSLINE
AN 1997:14146 AIDSLINE
DN MED-97216825
TI [Effect of saponins from Hedera taurica Carr. and modified muramylpeptides on replication of human immunodeficiency virus in vitro].
Vliianie saponinov iz Hedera taurica Carr. i modifitsirovannykh muramilpeptidov na reproduksiiu virusa immunodefitsita cheloveka in vitro.
AU Krivorutchenko IuL; Andronovskaia I B; Chirva VIa; Pertel' S S; Grishkovets V I; Zemliakov A E; Kur'ianov V O; Krivoshein IuS
SO VOPROSY VIRUSOLOGII, (1997). Vol. 42, No. 1, pp. 34-6.
Journal code: XL8. ISSN: 0507-4088.
CY RUSSIA: Russian Federation
DT Journal; Article; (JOURNAL ARTICLE)
FS MED; Priority Journals
LA Russian
SL English
OS MEDLINE 97216825

EM 199706
AB The effects of muramyl dipeptide (MDP), several new MDP derivatives, and saponins derived from *Hedera taurica* Carr, on the in vitro replication of HIV-1 were studied. The coefficient of alteration of the rate of HIV replication was used to compare these reagents' effects on virus replication in Jurkat-tat cells. This coefficient was calculated as the ratio of concentrations of HIV p24 in supernatants to the amount of viable cells. Muramyl peptides boosted HIV replication. Only one modified muramyl peptide alpha-butyl-MDP and tauroside H2 were not capable of boosting HIV-1 antigen production.

CT Check Tags: Human
***Acetylmuramyl-Alanyl-Isoglutamine: PD, pharmacology**
Culture Media
English Abstract
HIV Core Protein p24: AN, analysis
*HIV-1: DE, drug effects
HIV-1: PH, physiology
Jurkat Cells
*Plants: CH, chemistry
*Saponins: PD, pharmacology
*Virus Replication: DE, drug effects

RN **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine)**
CN 0 (Culture Media); 0 (HIV Core Protein p24); 0 (Saponins)

L76 ANSWER 5 OF 38 AIDSLINE
AN 1996:2606 AIDSLINE
DN MED-96002631
TI Induction of a CD8+ cytotoxic T lymphocyte response to soluble antigen given together with a novel muramyl dipeptide adjuvant, N-acetyl-D-glucosaminyl-(beta 1-4)-N-acetylmuramyl-L-alanyl-D-isoglutamine (GMDP).

AU Hornung R L; Longo D L; Gowda V L; Kwak L W
CS Biological Carcinogenesis & Development Program, Program Resources, Inc./DynCorp, Frederick, MD, USA.
SO THERAPEUTIC IMMUNOLOGY, (1995). Vol. 2, No. 1, pp. 7-14.
Journal code: CCS. ISSN: 0967-0149.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
FS MED; Priority Journals
LA English
OS MEDLINE 96002631
EM 199601
AB We have investigated the ability of the novel muramyl dipeptide, GMDP, to act as an adjuvant for the induction of ovalbumin (OVA)-specific, CD8+ cytotoxic T lymphocyte (CTL) responses. C57Bl/6 mice were twice immunized s.c. with 50 micrograms OVA emulsified with a squalane, L121 pluronic containing Tween-80 vehicle either with (STP-GMDP) or without (STP) GMDP. Splenic precursor CD8+ CTL activity against E.G7-OVA, but not against EL-4 parental targets was detected in STP-GMDP immunized mice after 5 days of in vitro re-stimulation with irradiated E.G7-OVA cells, while mice immunized with OVA in STP alone or OVA alone failed to demonstrate CTL activity. OVA emulsified in a microfluidized STP vehicle formulation without GMDP also elicited the E.G7-OVA precursor CTL. The ability of GMDP to induce a class I-restricted, CD8+ CTL response to a soluble protein antigen may have implications for the development of useful vaccines against viral pathogens or tumours against which CTL responses are desirable.

Acetylmuramyl-Alanyl-Isoglutamine: AA, analogs & derivatives

Adjuvants, Immunologic
 Antibodies, Monoclonal
 *Arthritis, Adjuvant: PA, pathology
 *Cyclosporine: TO, toxicity
 CD4-CD8 Ratio
 Flow Cytometry
 *Lymphocyte Subsets: DE, drug effects
 Rats
 Rats, Inbred Lew
 Spleen: CY, cytology
 *Spleen: DE, drug effects
 Tarsus, Animal: PA, pathology

RN **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine);** 59865-13-3
 (Cyclosporine); 78113-36-7 (romurtide)
 CN 0 (Adjuvants, Immunologic); 0 (Antibodies, Monoclonal)

L76 ANSWER 7 OF 38 AIDSLINE
 AN 1995:2784 AIDSLINE
 DN MED-95042886
 TI Synthesis of immunoadjuvant conjugates with HIV-derived peptide inducing peptide-specific antibody.
 AU Maruyama Y; Kurimura M; Achiwa K
 CS School of Pharmaceutical Sciences, University of Shizuoka, Japan.
 SO CHEMICAL AND PHARMACEUTICAL BULLETIN, (1994). Vol. 42, No. 8, pp. 1709-11.
 Journal code: CZP. ISSN: 0009-2363.
 CY Japan
 DT Journal; Article; (JOURNAL ARTICLE)
 FS MED
 LA English
 OS MEDLINE 95042886
 EM 199502
 CT Check Tags: Animal; Male

***Acetylmuramyl-Alanyl-Isoglutamine: AA, analogs & derivatives**

Acetylmuramyl-Alanyl-Isoglutamine: CS, chemical synthesis
Acetylmuramyl-Alanyl-Isoglutamine: IM, immunology
 Adjuvants, Immunologic: CH, chemistry
 *Adjuvants, Immunologic: CS, chemical synthesis
 Adjuvants, Immunologic: PD, pharmacology
 Amino Acid Sequence
 Antibody Specificity
 *AIDS Vaccines: IM, immunology
 Chromatography, High Pressure Liquid
 Enzyme-Linked Immunosorbent Assay
 *HIV Antibodies: BI, biosynthesis
 *HIV Envelope Protein gp120: IM, immunology
 *HIV-1: IM, immunology
 Mice
 Mice, Inbred BALB C
 Molecular Sequence Data
 Molecular Weight
 Peptide Fragments: CS, chemical synthesis
 Peptide Fragments: IM, immunology
 Vaccines, Synthetic: IM, immunology

RN **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine)**
 CN 0 (Adjuvants, Immunologic); 0 (AIDS Vaccines); 0 (HIV Antibodies); 0

(HIV Envelope Protein gp120); 0 (Peptide Fragments); 0 (Vaccines, Synthetic)

L76 ANSWER 8 OF 38 AIDSLINE
 AN 1995:2734 AIDSLINE
 DN MED-95052854
 TI Clinical and immunologic responses to human immunodeficiency virus (HIV) type 1SF2 gp120 subunit vaccine combined with MF59 adjuvant with or without muramyl tripeptide dipalmitoyl phosphatidylethanolamine in non-HIV-infected human volunteers.
 AU Kahn J O; Sinangil F; Baenziger J; Murcar N; Wynne D; Coleman R L; Steimer K S; Dekker C L; Chernoff D
 CS AIDS Program, San Francisco General Hospital, CA 94110.
 SO JOURNAL OF INFECTIOUS DISEASES, (1994). Vol. 170, No. 5, pp. 1288-91.
 Journal code: IH3. ISSN: 0022-1899.
 CY United States
 DT (CLINICAL TRIAL)
 (CLINICAL TRIAL, PHASE I)
 Journal; Article; (JOURNAL ARTICLE)
 (RANDOMIZED CONTROLLED TRIAL)
 FS MED; Abridged Index Medicus Journals; Priority Journals
 LA English
 OS MEDLINE 95052854
 EM 199502
 AB A phase 1 study of 42 non-human immunodeficiency virus type 1 (HIV)-infected volunteers was initiated to determine the safety and immunogenicity of an HIV subunit vaccine consisting of recombinant envelope gp120 derived from HIVSF2 (rgp120SF2) combined with a novel adjuvant, MF59, with or without the immunomodulator muramyl tripeptide dipalmitoyl phosphatidylethanolamine (MTP-PE). All injections contained adjuvant MF59, and subjects were grouped according to MTP-PE dose. Injections were given on days 0, 30, 180, and 365. The vaccine was well tolerated with limited local and systemic reactions. These immunizations induced rgp120SF2-specific binding antibodies that persisted > or = 24 weeks. After three immunizations, all subjects receiving the antigen developed neutralizing antibodies to HIVSF2, and serum from 67% of these subjects also cross-neutralized HIVMN. ELISA-reactive antibodies to the HIVSF2 V3 region and strong lymphoproliferative responses to HIVSF2 envelope proteins were detected in all rgp120SF2-immunized subjects.
 CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't
***Acetylmuramyl-Alanyl-Isoglutamine: AA, analogs & derivatives**
Acetylmuramyl-Alanyl-Isoglutamine: AD, administration & dosage
 *Adjuvants, Immunologic: AD, administration & dosage
 Adolescence
 Adult
 AIDS Vaccines: AD, administration & dosage
 *AIDS Vaccines: IM, immunology
 Double-Blind Method
 HIV Antibodies: BL, blood
 *HIV Envelope Protein gp120: IM, immunology
 Immunization
 Middle Age
 *Phosphatidylethanolamines: AD, administration & dosage
 *Polysorbates: AD, administration & dosage

Acetylmuramyl-Alanyl-Isoglutamine: AD, administration & dosage

Acetylmuramyl-Alanyl-Isoglutamine: IM, immunology

*Adjuvants, Immunologic

Adjuvants, Immunologic: AD, administration & dosage

AIDS Vaccines: AD, administration & dosage

*AIDS Vaccines: IM, immunology

Cytotoxicity, Immunologic

Drug Carriers

*Gene Products, env: IM, immunology

HIV Antibodies: BI, biosynthesis

*HIV-1: IM, immunology

Interleukin-7: AD, administration & dosage

*Interleukin-7: IM, immunology

Liposomes

Mice

Mice, Inbred C3H

Phosphatidylethanolamines: AD, administration & dosage

*Phosphatidylethanolamines: IM, immunology

Recombinant Proteins: AD, administration & dosage

Recombinant Proteins: IM, immunology

Specific Pathogen-Free Organisms

T-Lymphocytes, Cytotoxic: IM, immunology

Vaccines, Synthetic: AD, administration & dosage

Vaccines, Synthetic: IM, immunology

RN **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine);** 83461-56-7
(CGP 19835 A)

CN 0 (Adjuvants, Immunologic); 0 (AIDS Vaccines); 0 (Drug Carriers); 0
(Gene Products, env); 0 (HIV Antibodies); 0 (Interleukin-7); 0
(Liposomes); 0 (Phosphatidylethanolamines); 0 (Recombinant
Proteins); 0 (Vaccines, Synthetic)

L76 ANSWER 10 OF 38 AIDSLINE

AN 1994:6961 AIDSLINE

DN MED-94235370

TI Immune responses induced by prototype vaccines for AIDS in rhesus
monkeys.

AU Ohkawa S; Wilson L A; Larosa G; Javaherian K; Martin L N;
Murphey-Corb M

CS Department of Microbiology, Tulane Regional Primate Research Center,
Covington, Louisiana 70433.

NC N01-AI-62560 (NIAID)

N01-AI-15093 (NIAID)

P51-RR-00164 (NCRR)

+

SO AIDS RESEARCH AND HUMAN RETROVIRUSES, (1994). Vol. 10, No. 1, pp.
27-38.

Journal code: ART. ISSN: 0889-2229.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

FS MED; Priority Journals

LA English

OS MEDLINE 94235370

EM 199408

AB A battery of assay systems was used to profile both humoral and
cell-mediated immune responses induced by immunization with
candidate vaccines consisting of recombinant simian immunodeficiency
virus (SIV) glycoproteins rgp110 (nondenatured) with SAF-M adjuvant
(gp110 + SAF-M) or rgp140 (denatured) with Freund's adjuvant (gp140

CN 0 (Antibodies, Viral); 0 (AIDS Vaccines); 0 (IgG); 0 (Polysorbates);
0 (Retroviridae Proteins); 0 (Syntex adjuvant formulation); 0 (SIV
envelope protein gp110); 0 (Vaccines, Synthetic); 0 (Viral Envelope
Proteins)

L76 ANSWER 11 OF 38 AIDSLINE

AN 1993:15331 AIDSLINE

DN ICA9-93335772

TI Effect of muramyl peptides on replication of human immunodeficiency
virus in combination with antiretrovirals.

AU Masihi K N; Chedid L

CS Robert Koch Institute, Berlin, Germany.

SO Int Conf AIDS, (1993). Vol. 9, No. 1, pp. 494 (Abstract No.
PO-B28-2154).

CY GERMANY: Germany, Federal Republic of

DT Abstract

FS ICA9

LA English

EM 199311

AB Efforts to improve the hematologic tolerance of AZT and related
compounds have led to the application of CSFs. Immunomodulator MDP
can enhance monocyte-macrophage CSF in serum, induce a proliferation
of multipotential stem cells in the bone marrow and increase the
numbers of granulocyte-macrophage progenitors in the spleen. MDP has
been shown possess an inhibitory activity against HIV infection of
CD4-positive cells. In the present study, the effect of the
combination of MDPs with suboptimal doses of ddC, AZT and IFN-gamma,
were investigated. A significant synergistic activity against HIV
infection of U937 cells was obtained using MDP, muradimetide, or
murametide in combination with a suboptimal dose of AZT, ddC
or a low-activity dose of interferon-gamma. Surprising synergistic
activity was obtained using muradimetide in combination with even an
inactive dose of ddC.

CT Check Tags: Comparative Study; Human

***Acetylmuramyl-Alanyl-Isoglutamine: PD, pharmacology**

*Adjuvants, Immunologic: PD, pharmacology

Drug Synergism

*HIV: DE, drug effects

HIV: PH, physiology

*Interferon Type II: PD, pharmacology

Monocytes: DE, drug effects

Monocytes: MI, microbiology

Tumor Cells, Cultured

*Virus Replication: DE, drug effects

*Zalcitabine: PD, pharmacology

*Zidovudine: PD, pharmacology

RN 30516-87-1 (Zidovudine); **53678-77-6 (Acetylmuramyl-Alanyl-
Isoglutamine)**; 7481-89-2 (Zalcitabine); 82115-62-6 (Interferon
Type II)

CN 0 (Adjuvants, Immunologic)

L76 ANSWER 12 OF 38 AIDSLINE

AN 1993:12996 AIDSLINE

DN ICA9-93336304

TI Phase 1 study of an HIV-1 gp 120 vaccine combined with MF59 and with
dose escalation of MTP-PE, in sero-negative adults.

AU Kahn J; Chernoff D; Sinangil F; Baenziger J; Murcar N; Steimer K

CS University of California San Francisco.

SO Int Conf AIDS, (1993). Vol. 9, No. 1, pp. 70 (Abstract No.

dosage**Acetylmuramyl-Alanyl-Isoglutamine: TO, toxicity**

Adjuvants, Immunologic: AD, administration & dosage

Adjuvants, Immunologic: TO, toxicity

Adult

*AIDS Vaccines: TO, toxicity

Double-Blind Method

HIV Envelope Protein gp120: IM, immunology

*HIV Envelope Protein gp120: TO, toxicity

*HIV-1: IM, immunology

Phosphatidylethanolamines: AD, administration & dosage

Phosphatidylethanolamines: TO, toxicity

*Vaccines, Synthetic: TO, toxicity

RN **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine);** 83461-56-7
(CGP 19835 A)

CN 0 (Adjuvants, Immunologic); 0 (AIDS Vaccines); 0 (HIV Envelope Protein gp120); 0 (Phosphatidylethanolamines); 0 (Vaccines, Synthetic)

L76 ANSWER 15 OF 38 AIDSLINE

AN 1993:9242 AIDSLINE

DN MED-93301828

TI Effects of adjuvants and multiple antigen peptides on humoral and cellular immune responses to gp160 of HIV-1.

AU Levi M; Ruden U; Birx D; Loomis L; Redfield R; Lovgren K; Akerblom L; Sandstrom E; Wahren B

CS Department of Virology, National Bacteriological Laboratory, Stockholm, Sweden.

SO JOURNAL OF ACQUIRED IMMUNE DEFICIENCY SYNDROMES, (1993). Vol. 6, No. 8, pp. 855-64.

Journal code: JOF. ISSN: 0894-9255.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

FS MED; Priority Journals

LA English

OS MEDLINE 93301828

EM 199309

AB The capacity of five different adjuvants, AlPO₄, a muramyldipeptide formulation (MDP.TSL), Freund's adjuvant, immunostimulating complex and its matrix components to elicit humoral and cellular responses in rabbits immunized with the human immunodeficiency virus type 1 (HIV-1) envelope protein rgp160IIIB was compared. The highest antibody titers against gp160 and gp41/gp120 epitopes were seen with rgp160 in MDP.TSL or Freund's adjuvant, whereas the broadest responses were seen in rabbits immunized with rgp160 in matrix or MDP.TSL. The broadest spectrum of high-avidity antibodies was also induced by rgp160 in MDP.TSL. Neutralizing titers against HIV-1IIIB, low titers to HIV-1MN, and the most efficient inhibition of viral cell-to-cell spread was seen with rgp160 in MDP.TSL. The strongest and most persisting cellular responses were induced by rgp160 in AlPO₄ or MDP.TSL. Using MDP.TSL as the adjuvant, we also improved the immune response against gp120 epitopes by boosting rgp160-primed rabbits with rgp160, multiple antigenic peptides (MAPs), or unconjugated peptides. The MAPs induced high neutralizing titers and were superior to rgp160 alone in inducing both humoral and cellular reactivity. MAPs are therefore strong candidates for inclusion into future HIV-1 vaccines.

CT Check Tags: Animal; Female

Acetylmuramyl-Alanyl-Isoglutamine: PD, pharmacology

*Adjuvants, Immunologic: PD, pharmacology
 Aluminum: PD, pharmacology
 Amino Acid Sequence
 Antibody Affinity
 Freund's Adjuvant: PD, pharmacology
 Gene Products, env: CH, chemistry
 *Gene Products, env: IM, immunology
 *HIV Antibodies: BI, biosynthesis
 HIV Antigens: CH, chemistry
 *HIV Antigens: IM, immunology
 HIV Envelope Protein gp41: IM, immunology
 *HIV-1: IM, immunology
 Immunity, Cellular: DE, drug effects
 Immunization
 Immunization, Secondary
 ISCOMs: IM, immunology
 ISCOMs: PD, pharmacology
 Lymphocyte Transformation: IM, immunology
 Molecular Sequence Data
 Peptide Fragments: CH, chemistry
 Peptide Fragments: IM, immunology
 Phosphates: PD, pharmacology
 Protein Precursors: CH, chemistry
 *Protein Precursors: IM, immunology
 Rabbits
 Recombinant Proteins: CH, chemistry
 Recombinant Proteins: IM, immunology
 T-Lymphocytes: IM, immunology
 Virus Replication: IM, immunology
 RN 13765-93-0 (aluminum phosphate); **53678-77-6**
 (**Acetylmuramyl-Alanyl-Isoglutamine**); 7429-90-5 (Aluminum);
 9007-81-2 (Freund's Adjuvant)
 CN 0 (Adjuvants, Immunologic); 0 (Gene Products, env); 0 (HIV
 Antibodies); 0 (HIV Antigens); 0 (HIV Envelope Protein gp160); 0
 (HIV Envelope Protein gp41); 0 (ISCOMs); 0 (Peptide Fragments); 0
 (Phosphates); 0 (Protein Precursors); 0 (Recombinant Proteins)
 L76 ANSWER 16 OF 38 AIDSLINE
 AN 1993:8499 AIDSLINE
 DN MED-93271840
 TI SIV vaccine protection of rhesus monkeys.
 AU Gardner M B; Carlson J R; Jennings M; Rosenthal A; Langlois A;
 Haynes B; Bolognesi D; Palker T J
 CS Department of Medical Pathology, University of California, Davis.
 SO BIOTECHNOLOGY THERAPEUTICS, (1991). Vol. 2, No. 1-2, pp. 9-19.
 Journal code: BNI. ISSN: 0898-2848.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 FS MED; Priority Journals
 LA English
 OS MEDLINE 93271840
 EM 199309
 AB Rhesus macaques (M. mulatta), immunized with an inactivated whole
 SIVmac vaccine and muramyl dipeptide or Freund's incomplete
 adjuvant, were protected against IV challenge infection with 10
 animal infectious doses of the homologous virus. The protection in
 these animals appeared to be complete, with no breakthrough of
 latent virus infection over a 10-month period. Vaccine protection in
 this model was correlated generally with a high level of SIVmac

envelope antibody by ELISA and immunoblot, high titers of syncytial inhibiting antibody, and, more specifically, with the presence of antibodies binding to a putative V3 loop synthetic peptide of the SIVmac outer envelope. This model can now be used for further identification of the protective epitopes and protective host immune responses as well as for development of novel and better AIDS vaccines.

CT Check Tags: Animal; Support, Non-U.S. Gov't

Acetylmuramyl-Alanyl-Isoglutamine: AD, administration & dosage

Antibodies, Viral: BI, biosynthesis

Antigens, Viral

Freund's Adjuvant: AD, administration & dosage

Gene Products, env: IM, immunology

Macaca mulatta

Neutralization Tests

Retroviridae Proteins, Oncogenic: IM, immunology

*Simian Acquired Immunodeficiency Syndrome: PC, prevention & control

*SIV: IM, immunology

Vaccines, Inactivated: AD, administration & dosage

Vaccines, Inactivated: PD, pharmacology

Viral Vaccines: AD, administration & dosage

*Viral Vaccines: PD, pharmacology

RN **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine); 9007-81-2**
(Freund's Adjuvant)

CN 0 (simian immunodeficiency virus transmembrane protein); 0
(Antibodies, Viral); 0 (Antigens, Viral); 0 (Gene Products, env); 0
(Retroviridae Proteins, Oncogenic); 0 (Vaccines, Inactivated); 0
(Viral Vaccines)

L76 ANSWER 17 OF 38 AIDSLINE

AN 1993:2935 AIDSLINE

DN MED-93103854

TI Comparison of protection afforded by whole virus ISCOM versus MDP adjuvanted formalin-inactivated SIV vaccines from IV cell-free or cell-associated homologous challenge.

AU Osterhaus A; de Vries P; Morein B; Akerblom L; Heeney J

CS Laboratory of Immunobiology, National Institute of Public Health and Environmental Protection, Bilthoven, The Netherlands.

SO AIDS RESEARCH AND HUMAN RETROVIRUSES, (1992). Vol. 8, No. 8, pp. 1507-10.

Journal code: ART. ISSN: 0889-2229.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

FS MED; Priority Journals

LA English

OS MEDLINE 93103854

EM 199303

AB A SIV-ISCOM and a SIV-MDP adjuvanted vaccine were tested for their potential to induce protection from intravenous cell-free or cell-associated homologous SIV challenge in rhesus monkeys (Macaca mulatta). Seven monkeys vaccinated four times over a four-month period with either the SIV-ISCOM or the SIV-MDP vaccine were challenged intravenously with approximately 10 MID50 cell-free SIVmac251 (32H). They all were protected from developing viremia during a three-month observation period. Two other groups of four monkeys were vaccinated essentially in the same way with either of these vaccines. They were challenged intravenously with approximately 10 MID50 of infected PBMC of a rhesus monkey that had

been infected with SIVmac251 (32H) 11 months earlier (stock prepared by J. Heeney). Two monkeys of each of these two groups proved to be protected from developing viremia during a two-month observation period. For both the cell-free and the cell-associated SIV challenge, monkeys vaccinated with measles virus ISCOMS or MDP adjuvanted measles virus antigen, served as controls. They all became viremic within two weeks after SIV challenge. This is the first demonstration that vaccinated previously unchallenged nonhuman primates can be protected from infection with lentivirus-infected PBMC from another animal. Serological analysis indicated that SIV-specific serum antibody titers were considerably higher in SIV-ISCOM vaccinated animals than in the SIV-MDP vaccinated animals. The serology also confirmed the protection data, by showing the absence of increase in SIV-specific serum antibodies in apparently protected animals after challenge.

CT Check Tags: Animal; Comparative Study; Support, Non-U.S. Gov't

***Acetylmuramyl-Alanyl-Isoglutamine: IM, immunology**

*Adjuvants, Immunologic

Antibodies, Viral: BI, biosynthesis

*ISCOMs: IM, immunology

Lymphocytes: MI, microbiology

Lymphocytes: TR, transplantation

Macaca mulatta: IM, immunology

*Simian Acquired Immunodeficiency Syndrome: PC, prevention & control

Simian Acquired Immunodeficiency Syndrome: TM, transmission

*SIV: IM, immunology

SIV: IP, isolation & purification

*Vaccines, Inactivated: IM, immunology

*Viral Vaccines: IM, immunology

RN **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine)**

CN 0 (Adjuvants, Immunologic); 0 (Antibodies, Viral); 0 (ISCOMs); 0 (Vaccines, Inactivated); 0 (Viral Vaccines)

L76 ANSWER 18 OF 38 AIDSLINE

AN 1993:2550 AIDSLINE

DN MED-93090458

TI The control of the antibody isotype response to recombinant human immunodeficiency virus gp120 antigen by adjuvants.

AU Bomford R; Stapleton M; Winsor S; McKnight A; Andronova T

CS Wellcome Research Laboratories, Beckenham, Kent, England.

SO AIDS RESEARCH AND HUMAN RETROVIRUSES, (1992). Vol. 8, No. 10, pp. 1765-71.

Journal code: ART. ISSN: 0889-2229.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

FS MED; Priority Journals

LA English

OS MEDLINE 93090458

EM 199303

AB Both saponin and muramyl dipeptide (MDP) formulated with a squalane-in-water emulsion of large particle size prepared with a vortex mixer were superior to Al(OH)₃ as adjuvants for HIV gp120 in mice. All the adjuvants induced IgG1 antibody, but saponin elicited the highest titers of IgG2a. The secretion of interleukin-5 (IL-5) and interferon gamma (IFN gamma) by lymph node cells cultured in vitro with gp120 was studied. All the cultures secreted IL-5, but only those from saponin-immunized mice produced IFN gamma, suggesting that saponin is capable of activating both the Th1 and Th2 T-cell subsets. The titers of neutralizing antibodies were low

with both MDP and saponin, and they occurred in mice which were also positive for antibodies against a V3 loop peptide. Glucosaminylmuramyl dipeptide (GMDP) which is less pyrogenic than MDP and a nonpyrogenic analog GMDPA, displayed equivalent adjuvant activity to MDP. The level and isotype composition of antibodies induced by GMDP in combination with squalane emulsions depended on the dimension of the emulsion particles. With a large (2500 nm) particle size the response was confined to IgG1 in Balb/c mice, but when this was reduced to 150 nm by sonication the antibody response was increased and relatively high levels of IgG2a appeared in some mice.

CT Check Tags: Animal; Comparative Study; Female; Male; Support, Non-U.S. Gov't

Acetylmuramyl-Alanyl-Isoglutamine: AD, administration & dosage

Adjuvants, Immunologic: AD, administration & dosage

Aluminum Hydroxide: AD, administration & dosage

*HIV Antibodies: BI, biosynthesis

HIV Envelope Protein gp120: AD, administration & dosage

*HIV Envelope Protein gp120: IM, immunology

*Immunoglobulin Isotypes: BI, biosynthesis

Interferon Type II: SE, secretion

Interleukin-5: SE, secretion

Mice

Mice, Inbred BALB C

Mice, Inbred CBA

Particle Size

Poloxalene: AD, administration & dosage

Recombinant Proteins: AD, administration & dosage

Recombinant Proteins: IM, immunology

Saponins: AD, administration & dosage

RN 21645-51-2 (Aluminum Hydroxide); **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine)**; 82115-62-6 (Interferon Type II); 9003-11-6 (Poloxalene)

CN 0 (Adjuvants, Immunologic); 0 (HIV Antibodies); 0 (HIV Envelope Protein gp120); 0 (Immunoglobulin Isotypes); 0 (Interleukin-5); 0 (Recombinant Proteins); 0 (Saponins)

L76 ANSWER 19 OF 38 AIDSLINE

AN 1993:1447 AIDSLINE

DN MED-93047471

TI Selection of a muramyl peptide based on its lack of activation of nuclear factor-kappa B as a potential adjuvant for AIDS vaccines.

AU Schreck R; Bevec D; Dukor P; Baeuerle P A; Chedid L; Bahr G M

CS Laboratorium fur Molekulare Biologie, Ludwig-Maximilians-Universitat, Martinsried, Germany.

SO CLINICAL AND EXPERIMENTAL IMMUNOLOGY, (1992). Vol. 90, No. 2, pp. 188-93.

Journal code: DD7. ISSN: 0009-9104.

CY ENGLAND: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)

FS MED; Priority Journals; Cancer Journals

LA English

OS MEDLINE 93047471

EM 199302

AB Activation of the cellular transcription factor nuclear factor-kappa B (NF-kappa B) by cytokines and other immunostimulants has been tightly linked with enhanced replication of human immunodeficiency virus-type 1 (HIV-1) in infected cells. Various immunomodulators are

L76 ANSWER 24 OF 38 AIDSLINE
 AN 1992:8223 AIDSLINE
 DN MED-92287545
 TI Impaired stimulation of anti-bovine serum albumin IgG antibodies by vaccine adjuvants in murine acquired immunodeficiency syndrome.
 AU Phillips N C
 CS Montreal General Hospital Research Institute, Quebec, Canada.
 SO FEMS MICROBIOLOGY IMMUNOLOGY, (1992). Vol. 4, No. 4, pp. 209-18.
 Journal code: AO3. ISSN: 0920-8534.
 CY Netherlands
 DT Journal; Article; (JOURNAL ARTICLE)
 FS MED; Priority Journals
 LA English
 OS MEDLINE 92287545
 EM 199209
 AB The effect of three adjuvants - alum, N-acetylmuramyl-L-alanyl-D-isoglutamine (MDP), and liposomes - on the IgG antibody isotype response to bovine serum albumin (BSA), was determined in normal and LP-BM5 retrovirus infected C57BL/6 mice. Alum and MDP induced comparable levels of IgG antibodies in normal mice (predominantly IgG1 (greater than 90%)), whereas liposomes induced IgG1 (60%), IgG2a/b (30%) and IgG3 (10%) antibodies. IgG antibody levels using liposomes as adjuvant were five-fold higher than those observed with alum or MDP. Immunization after LP-BM5 infection significantly reduced the effectiveness of alum and MDP, IgG antibody levels being reduced by 80 and 90% at 3 or 7 weeks respectively. The adjuvant activity of liposomes was reduced by 55 and 65% when immunization was started 3 or 7 weeks post LP-BM5 infection. Boosting of pre-immune mice with BSA and alum, MDP or liposomes 3 weeks after LP-BM5 infection showed that, while the magnitude of the antibody response and isotype distribution was not affected, the persistence of the response was severely diminished compared to control, non-infected mice. The reduced immunoadjuvant activity correlated with a reduction in the frequency of splenic Thyl.2+/CD4+ T cells. These results demonstrated that liposomes were more effective than alum or MDP in inducing IgG antibodies, and that immunoadjuvant activity for prophylactic or therapeutic immunization for all 3 adjuvants was significantly impaired by retroviral infections.
 CT Check Tags: Animal; Comparative Study; Female
 Acetylmuramyl-Alanyl-Isoglutamine: IM, immunology
 Acetylmuramyl-Alanyl-Isoglutamine: PD, pharmacology
 *Adjuvants, Immunologic: PD, pharmacology
 Alum Compounds: PD, pharmacology
 *IgG: BI, biosynthesis
 Immunoglobulin Isotypes: BI, biosynthesis
 Immunologic Memory
 Liposomes: IM, immunology
 Mice
 Mice, Inbred C57BL
 *Murine Acquired Immunodeficiency Syndrome: IM, immunology
 Serum Albumin, Bovine: IM, immunology
 T-Lymphocyte Subsets: IM, immunology
 RN 10043-01-3 (aluminum sulfate); **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine)**
 CN 0 (Adjuvants, Immunologic); 0 (Alum Compounds); 0 (IgG); 0 (Immunoglobulin Isotypes); 0 (Liposomes); 0 (Serum Albumin, Bovine)

 L76 ANSWER 25 OF 38 AIDSLINE
 AN 1992:6924 AIDSLINE

DN PRIM9-1680292
TI Vaccine protection of rhesus macaques against SIVmac infection by high but not low doses of inactivated whole SIVmac immunogen.
AU Hartung S; Norley S; Bourquin P; Ennen J; Kurth R
CS Paul-Ehrlich-Institut, Paul-Ehrlich-Str. 51 - 59, 6070 Langen.
SO Symp Nonhum Primate Models AIDS, (1991). Vol. 9, pp. 121 (Abstract No. 102).
CY United States
DT Abstract
FS PRIM9
LA English
EM 199208
AB Eight Rhesus macaques were immunized intramuscularly four times (0, 1, 2, 4 months) over a period of 4 months with a formalin inactivated whole SIV vaccine in the presence of muramyl dipeptide (MDP) as adjuvant. Four animals received 0.5 mg and the other four 0.1 mg immunogen per injection. Three weeks after the final immunization the vaccinated monkeys along with two control monkeys were challenged intravenously with 10-50 MID50 of SIVmac251-32H. At the time of challenge 3 out of 4 animals of the high dose group has high titers (greater than 1:400) of antibody able to neutralize in vitro the homologous 32H strain of SIVmac. All other animals had low but measurable titers (1:50 - 1:200) of neutralizing antibody. The status of other immune parameters will be presented. Upon challenge three of the four animals from the low dose group (plus the nonvaccinated control animals) became infected as demonstrated by reisolation of virus from PBMC taken at two weeks post challenge and the development of a strong anamnestic response to SIVmac antigen. All other animals (one from low dose group and all four of the high dose group) remain negative by both parameters. These data indicate that when used in conjunction with MDP, the amount of immunogen required per immunization is between 0.1 and 0.5 mg. In addition, there is no apparent correlation between protection and the levels of homologous neutralizing antibody.
CT Check Tags: Animal
Acetylmuramyl-Alanyl-Isoglutamine: AD, administration & dosage
Antibodies, Viral: AN, analysis
Antigens, Viral: IM, immunology
Macaca mulatta
Neutralization Tests
*SIV: IM, immunology
*Vaccines, Inactivated: AD, administration & dosage
*Vaccines, Synthetic: AD, administration & dosage
RN **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine)**
CN 0 (Antibodies, Viral); 0 (Antigens, Viral); 0 (Vaccines, Inactivated); 0 (Vaccines, Synthetic)

L76 ANSWER 26 OF 38 AIDSLINE
AN 1992:4566 AIDSLINE
DN MED-92182252
TI Adjuvant formulations and their mode of action.
AU Allison A C; Byars N E
CS Syntech Research, Palo Alto, CA 94304.
SO SEMINARS IN IMMUNOLOGY, (1990). Vol. 2, No. 5, pp. 369-74.
Journal code: A61. ISSN: 1044-5323.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
FS MED; Priority Journals

LA English
 OS MEDLINE 92182252
 EM 199206
 AB We have developed an adjuvant formulation (SAF) consisting of a synthetic muramyl dipeptide analogue (N-acetylmuramyl-L-threonyl-D-isoglutamine) in a squalane-Pluronic polymer emulsion. Used with a variety of antigens SAF elicits cell-mediated immunity and antibodies of protective isotypes (IgG2a in the mouse). SAF augments responses to influenza virus haemagglutinin and hepatitis B virus surface antigen. Vaccines using SAF have protected guinea pigs against genital herpes simplex virus infections and subhuman primates against Epstein-Barr virus and simian immunodeficiency virus infections. Properties of SAF are compared with those of other adjuvants, including lipopolysaccharide analogs, ISCOMs and liposomes.
 CT Check Tags: Animal
 ***Acetylmuramyl-Alanyl-Isoglutamine: AA, analogs & derivatives**
 Acetylmuramyl-Alanyl-Isoglutamine: IM, immunology
 *Adjuvants, Immunologic
 Adjuvants, Immunologic: CH, chemistry
 *Antigens, Viral: IM, immunology
 Emulsions
 Guinea Pigs
 Haplorhini
 Hepatitis B Virus: IM, immunology
 Herpesvirus 4, Human: IM, immunology
 Immunity, Cellular
 *Immunotherapy, Active
 Mice
 Orthomyxoviridae: IM, immunology
 Simplexvirus: IM, immunology
 SIV: IM, immunology
 *Vaccines: IM, immunology
 RN **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine);** 66112-59-2
 (N-acetylmuramyl-threonyl-isoglutamine)
 CN 0 (Adjuvants, Immunologic); 0 (Antigens, Viral); 0 (Emulsions); 0 (Vaccines)

 L76 ANSWER 27 OF 38 AIDSLINE
 AN 1991:4933 AIDSLINE
 DN MED-91175188
 TI Vaccine protection of rhesus macaques against simian immunodeficiency virus infection.
 AU Carlson J R; McGraw T P; Keddie E; Yee J L; Rosenthal A; Langlois A J; Dickover R; Donovan R; Luciw P A; Jennings M B; et al
 CS Department of Pathology, School of Medicine, University of California, Davis 95616.
 NC AI25900 (NIAID)
 AI26471 (NIAID)
 SO AIDS RESEARCH AND HUMAN RETROVIRUSES, (1990). Vol. 6, No. 11, pp. 1239-46.
 Journal code: ART. ISSN: 0889-2229.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 FS MED; Priority Journals
 LA English
 OS MEDLINE 91175188
 EM 199107

glycoprotein (gp31). Protected monkeys tended to have higher titers of syncytial inhibition antibody prior to challenge. An anamnestic response after challenge was observed only in the vaccinated monkeys that became infected. Vaccinated animals that became challenge-infected tended to live longer than infected controls. These results confirm those at other primate centers and indicate that killed whole SIV vaccines can protect against low challenge doses of SIV and prevent early death in those monkeys that do become infected. The mechanism of this protection remains undetermined. Initial results from a cross-challenge experiment done in collaboration with Dr. Murphey-Corb (Delta Regional Primate Research Center) indicate that SIVmac immunized monkeys are protected against IV challenge with 10 ID of SIVsm and, conversely, SIVsm immunized monkeys are protected against IV challenge with 10 ID of SIVmac. These two SIV strains differ by about 17% in envelope sequences indicating that the vaccine induced protection appears to be fairly broad. These findings add optimism to the possibility of an eventual AIDS vaccine.

CT Check Tags: Animal

***Acetylmuramyl-Alanyl-Isoglutamine: IM, immunology**

Antibodies, Viral: BI, biosynthesis

Cells, Cultured

Dose-Response Relationship, Immunologic

*Freund's Adjuvant

Leukocytes, Mononuclear: MI, microbiology

Macaca mulatta

*Simian Acquired Immunodeficiency Syndrome: PC, prevention & control

SIV: GD, growth & development

*SIV: IM, immunology

Viral Envelope Proteins: IM, immunology

*Viral Vaccines

Virus Activation: IM, immunology

RN **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine); 9007-81-2**

(Freund's Adjuvant)

CN 0 (Antibodies, Viral); 0 (Viral Envelope Proteins); 0 (Viral Vaccines)

L76 ANSWER 31 OF 38 AIDSLINE

AN 1991:3441 AIDSLINE

DN MED-91108143

TI Safety and immunogenicity of a genetically engineered human immunodeficiency virus vaccine.

AU Wintsch J; Chagnat C L; Braun D G; Jeannet M; Stalder H; Abrignani S; Montagna D; Clavijs F; Moret P; Dayer J M; et al

CS Department of Medicine, University Hospital, Geneva, Switzerland.

NC AI-22778 (NIAID)

SO JOURNAL OF INFECTIOUS DISEASES, (1991). Vol. 163, No. 2, pp. 219-25.

Journal code: IH3. ISSN: 0022-1899.

CY United States

DT (CLINICAL TRIAL)

Journal; Article; (JOURNAL ARTICLE)

FS MED; Abridged Index Medicus Journals; Priority Journals

LA English

OS MEDLINE 91108143

EM 199105

AB A phase 1 trial of a candidate human immunodeficiency virus type 1 (HIV-1) vaccine was done in 25 healthy seronegative subjects. The antigen, env2-3 (SF2), was a nonglycosylated polypeptide representing the gp120 region of the env gene of the HIV-1(SF2)

isolate. It was produced in genetically engineered yeast as a denatured molecule incapable of binding CD4. A synthetic lipophilic muramyl tripeptide (MTP-PE) was used as an adjuvant. Ten subjects received adjuvant alone and 15 received 50- or 250-micrograms doses of env2-3 (SF2) administered intramuscularly in two immunization regimens. In general, adjuvant and vaccine were well tolerated. Antibody responses to both the homologous antigen, env2-3 (SF2), and antigens from other highly divergent HIV isolates were elicited in the majority of vaccine recipients. However, antibody titers were low, without neutralizing activity. In 9 of 11 subjects who received the complete vaccine immunization series, a significant specific T lymphocyte response was observed.

CT Check Tags: Human; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.

Acetylmuramyl-Alanyl-Isoglutamine: AA, analogs & derivatives

Acetylmuramyl-Alanyl-Isoglutamine: AE, adverse effects

Acetylmuramyl-Alanyl-Isoglutamine: IM, immunology

Adjuvants, Immunologic: AE, adverse effects

Adult

Antiviral Agents: AE, adverse effects

Antiviral Agents: IM, immunology

Blotting, Western

Drug Evaluation

Drug Tolerance

Enzyme-Linked Immunosorbent Assay

HIV Antibodies: BI, biosynthesis

HIV Envelope Protein gp120: IM, immunology

*HIV-1: IM, immunology

Immunoblotting

Leukocytes, Mononuclear: IM, immunology

Lymphocyte Transformation

Middle Age

Phosphatidylethanolamines: AE, adverse effects

Phosphatidylethanolamines: IM, immunology

T-Lymphocytes: IM, immunology

Vaccines, Synthetic: AE, adverse effects

Vaccines, Synthetic: IM, immunology

Viral Vaccines: AE, adverse effects

*Viral Vaccines: IM, immunology

RN **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine);** 83461-56-7
(CGP 19835 A)

CN 0 (Adjuvants, Immunologic); 0 (Antiviral Agents); 0 (HIV Antibodies); 0 (HIV Envelope Protein gp120); 0 (Phosphatidylethanolamines); 0 (Vaccines, Synthetic); 0 (Viral Vaccines)

L76 ANSWER 32 OF 38 AIDSLINE

AN 1991:1828 AIDSLINE

DN MED-91069612

TI The lipophilic muramyl peptide MTP-PE is a potent inhibitor of HIV replication in macrophages.

AU Lazdins J K; Woods-Cook K; Walker M; Alteri E

CS CIBA-GEIGY Limited Basel, Pharma Research Laboratories, Switzerland.

SO AIDS RESEARCH AND HUMAN RETROVIRUSES, (1990). Vol. 6, No. 10, pp. 1157-61.

Journal code: ART. ISSN: 0889-2229.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

AB OBJECTIVE: To develop adjuvant formulations suitable for human vaccine use that surpass alum in their ability to enhance immunity to HIV-1 subunit immunogens. METHODS: A series of adjuvant formulations consisting of MTP-PE in metabolizable oil emulsions have been compared to conventional adjuvants such as alum and Freund's. Experimental animals were immunized with recombinant HIV-1 gp120 antigens (both non-glycosylated denatured and fully glycosylated native versions) in the various formulations, their sera were tested for ELISA-reactive and virus neutralizing antibodies and their helper T cell responses were assessed by lymphoproliferative assays. RESULTS: Most of these novel adjuvant formulations were effective in guinea pigs, mice and rabbits. However, the properties of the emulsion dramatically influenced the efficacy of these formulations in larger animals such as goats and baboons. One new formulation was as effective as Freund's incomplete adjuvant and was also at least 10-fold more effective than alum in enhancing antibody responses, neutralizing antibody titers and lymphoproliferative responses to recombinant gp120 antigens in large animals. CONCLUSIONS: Improved adjuvants with the potential of enhancing immune responses to recombinant HIV-1 gp120 antigens in humans have been developed. Further immunogenicity studies and extensive safety trials with these formulations are in progress.

CT Check Tags: Animal

Acetylmuramyl-Alanyl-Isoglutamine: AA, analogs & derivatives

***Acetylmuramyl-Alanyl-Isoglutamine: PD, pharmacology**

*Adjuvants, Immunologic

*HIV Antibodies: BI, biosynthesis

*HIV Envelope Protein gp120: IM, immunology

*HIV-1: IM, immunology

Immunization

*Recombinant Proteins: IM, immunology

RN 64374-58-9 (muramyl tripeptide)

CN 0 (Adjuvants, Immunologic); 0 (HIV Antibodies); 0 (HIV Envelope Protein gp120); 0 (Recombinant Proteins)

L76 ANSWER 34 OF 38 AIDSLINE

AN 1990:7260 AIDSLINE

DN MED-90253926

TI Muramyl dipeptide inhibits replication of human immunodeficiency virus in vitro.

AU Masihi K N; Lange W; Rohde-Schulz B; Chedid L

CS Robert Koch Institute, Federal Health Office, West Berlin, Germany.

SO AIDS RESEARCH AND HUMAN RETROVIRUSES, (1990). Vol. 6, No. 3, pp. 393-9.

Journal code: ART. ISSN: 0889-2229.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

FS MED; Priority Journals

LA English

OS MEDLINE 90253926

EM 199008

AB In the search for compounds capable of inducing endogenous production of colony-stimulating factor (CSF) and possessing activity against human immunodeficiency virus (HIV), an immunomodulator, muramyl dipeptide (MDP), was investigated. MDP can enhance monocyte-macrophage CSF in serum and promote nonspecific resistance against a variety of microbial pathogens. MDP exhibited an inhibitory activity against HIV infection of CD4+ H9 lymphocytes

and U937 monocytoid cells. An inhibitor of viral reverse transcriptase, 2', 3'-dideoxyadenosine, produced potent inhibition in cultures which were similarly infected with HIV. MDP could partially reduce antigen production in persistently HIV-infected KE37/1 lymphocyte cultures.

CT Check Tags: Human

***Acetylmuramyl-Alanyl-Isoglutamine: PD, pharmacology**
 Cells, Cultured
 Colony-Stimulating Factors: BI, biosynthesis
 Dideoxyadenosine: PD, pharmacology
 Gene Products, gag: BI, biosynthesis
 *HIV: DE, drug effects
 HIV: GD, growth & development
 Viral Core Proteins: BI, biosynthesis
 *Virus Replication: DE, drug effects

RN 4097-22-7 (Dideoxyadenosine); **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine)**

CN 0 (Colony-Stimulating Factors); 0 (Gene Products, gag); 0 (HIV Core Protein p24); 0 (Viral Core Proteins)

L76 ANSWER 35 OF 38 AIDSLINE
 AN 1990:3642 AIDSLINE
 DN MED-90155807
 TI Exacerbation of human immunodeficiency virus infection in promonocytic cells by bacterial immunomodulators.
 AU Masihi K N; Lange W; Rohde-Schulz B
 CS Robert Koch Institute, Federal Health Office, Berlin, F.R.G.
 SO JOURNAL OF ACQUIRED IMMUNE DEFICIENCY SYNDROMES, (1990). Vol. 3, No. 3, pp. 200-5.
 Journal code: JOF. ISSN: 0894-9255.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 FS MED; Priority Journals
 LA English
 OS MEDLINE 90155807
 EM 199005

AB Common bacterial infections are increasingly being diagnosed in HIV-infected individuals. Cells of the monocyte-macrophage lineage kill invading bacterial pathogens and subsequently release immunoadjuvant components from the degraded cell walls. Since monocytes can be infected with HIV, effects of bacterial immunomodulators on infected promonocytic U937 cells were investigated. Synthetic muramyl peptide, mycobacterial trehalose dimycolate, and detoxified endotoxin exhibited an initial reduction followed by a rapid increase in HIV p24 antigen production. The upregulation of virus expression was correlated with enhanced interleukin-1 beta levels and a decrease in TNF-alpha production.

CT Check Tags: Human

***Acetylmuramyl-Alanyl-Isoglutamine: PD, pharmacology**
 Cell Line
 *Cord Factors: PD, pharmacology
 Dideoxyadenosine: PD, pharmacology
 *Glycolipids: PD, pharmacology
 HIV-1: DE, drug effects
 *HIV-1: PH, physiology
 Interferon Type II: PD, pharmacology
 Interleukin-1: BI, biosynthesis
 *Lipid A: AA, analogs & derivatives
 Lipid A: PD, pharmacology

Blood, Blood-Forming Organs and Body Fluids-Lymphatic Tissue and
Reticuloendothelial System *15008
Pharmacology-Immunological Processes and Allergy *22018
Immunology and Immunochemistry-Immunopathology, Tissue Immunology
*34508
Medical and Clinical Microbiology-Virology *36006
Chemotherapy-Antiviral Agents *38506

BC **Retroviridae 02623**

=> d all 14 2

L4 ANSWER 2 OF 2 BIOSIS COPYRIGHT 1998 BIOSIS
AN 96:361435 BIOSIS
DN 99083791
TI Enhancement by muramyl peptides of the protective response of
interferon-alpha-beta against encephalomyocarditis virus infection.
AU Pouillart P R; Audibert F M; Chedid L A; LeFrancier P L; Bahr G M
CS VACSYN S.A., 33 Boulevard du General Martial Valin, 75015 Paris,
France
SO International Journal of Immunopharmacology 18 (3). 1996. 183-192.
ISSN: 0192-0561
LA English
PR Biological Abstracts Vol. 102 Iss. 004 Ref. 049240
AB The use of interferon-alpha (IFN-alpha) in the treatment of
infectious diseases has shown limited efficacy and dose-limiting
toxicity. We have selected safe immunomodulators of the muramyl
peptide family with the potential of enhancing the efficacy of
IFN-alpha without resulting in increased toxicity. One of these
synthetic muramyl dipeptide (MDP) derivatives, namely
murabutide which is in a clinical stage of development, has
been recently found to synergize with IFN-alpha-2a in the selective
induction of anti-inflammatory mediators and to enhance the
biological activities of the therapeutic cytokine. The present study
was performed to assess the antiviral activity of such muramyl
peptides and a possible potentiation of the antiviral activity of
IFN-alpha/beta by associated therapy using the classical assay of
Encephalomyocarditis virus (EMCV) infection. In vitro, pretreatment
of Moloney Sarcoma virus (MSV)-transformed cell line with MDP
derivatives followed by treatment with IFN-alpha/beta showed a
synergistic protection against the cytopathogenic effect of a
subsequent EMCV infection. None of the MSV cultures could be
protected by stimulation with muramyl peptides alone. In vivo, all of
the muramyl peptide derivatives tested were found to be more potent
than the parent molecule MDP in inducing protection against death or
in the prolongation of the mean survival time of infected mice.
Sequential administration of suboptimal doses of exogenous
IFN-alpha/beta and muramyl peptides established a strong antiviral
state and considerably improved the protective effect of the
cytokine, frequently leading to an abortive infection. Our findings
suggest that combination therapy with safe muramyl peptides and
IFN-alpha/beta could constitute a highly effective and new regimen
for the treatment of viral infections in humans.
ST RESEARCH ARTICLE; MOUSE; **MURABUTIDE**; IMMUNOLOGIC-DRUG;
MOLONEY SARCOMA VIRUS; INTERFERON-ALPHA; ANTIVIRAL-DRUG;
HORMONE-DRUG; INTERFERON-BETA; ANTIVIRAL-DRUG; HORMONE-DRUG;
CYTOKINE; TOXICITY; POTENTIAL CLINICAL APPLICATION
RN **74817-61-1** (MURABUTIDE)
CC Biochemical Studies-Proteins, Peptides and Amino Acids 10064

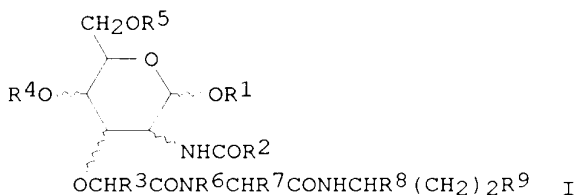
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as drug for enhancing host resistance against
opportunistic infections in **AIDS** patients)

L62 ANSWER 21 OF 23 HCAPLUS COPYRIGHT 1998 ACS
AN 1990:112072 HCAPLUS
DN 112:112072
TI Dipeptidyl saccharides as host resistance enhancers in **AIDS**
-immuno-compromised hosts and methods of use
IN Durette, Philippe L.
PA Merck and Co., Inc., USA
SO U.S., 19 pp.
CODEN: USXXAM

DT **Patent**
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 4866035	A	19890912	US 87-105056	19871005
OS	MARPAT 112:112072				
GI					



AB The dipeptidylsaccharides I [R₁ = H, (un)substituted alkyl, alkoxy, etc.; R₂ = (un)substituted alkyl, alkoxy, alkylmercapto, etc.; R₃ = H, alkyl; R₄, R₅ = H, alkanoyl, benzoyl, naphthoyl, etc.; R₆ = H; R₆R₇ = CH₂CH₂CH₂; R₈, R₉ = CO₂H, alkoxycarbonyl, (un)substituted CONH₂, etc.] are prepd. as agents for enhancing host resistance to opportunistic bacterial, viral or fungal infections in **AIDS** patients. I help to suppress the **AIDS** virus infection itself. A soln. of benzyl 2-acetamido-4,6-O-benzylidene-2-deoxy-3-O-(D-2-propionyl-L-alanyl-D-isoglutamine benzyl ester)-.alpha.-D-galactopyranoside (prepn. given) in HOAc was hydrogenolyzed over Pd black, to give 2-acetamido-2-deoxy-3-O-(D-2-propionyl-L-alanyl-D-isoglutamine)-D-galactose. I (no specific compd. given), injected i.p., at 100-300 mg/kg, to mice immunized with BSA (bovine serum albumin), increased the prodn. of anti-BSA antibodies. I may be administered jointly with known antiviral anti-**AIDS** drugs, such as azidothymidine, ansamycin, ribavirin, etc.

IT **69351-74-2P 75283-22-6P 75283-24-8P**
76465-71-9P 76497-96-6P 76498-00-5P
87420-93-7P 125637-73-2P 125637-74-3P

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as host resistance enhancer, in **AIDS**)

L62 ANSWER 22 OF 23 HCAPLUS COPYRIGHT 1998 ACS
AN 1987:605162 HCAPLUS
DN 107:205162

lymphocyte cultures.

IT **53678-77-6**, Muramyl dipeptide
 RL: BIOL (Biological study)
 (human immunodeficiency virus replication in
 infected cells inhibition by)

L62 ANSWER 20 OF 23 HCAPLUS COPYRIGHT 1998 ACS

AN 1990:112074 HCAPLUS

DN 112:112074

TI Preparation of dipeptidyl-2-amino-1,2-dideoxy-D-glucose derivatives
 as host resistance enhancers in **AIDS**-immunocompromised
 hosts and methods of use

IN Durette, Philippe L.

PA Merck and Co., Inc., USA

SO U.S., 11 pp.

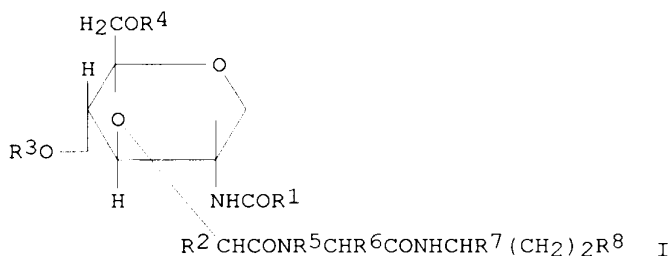
CODEN: USXXAM

DT **Patent**

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	US 4868157	A	19890919	US 87-105051	19871005
GI					



AB The title compds. [R₁ = (un)substituted alkyl or Ph; R₂ = H, alkyl; R₃, R₄ = H, acyl, R₁₁(CO)nX(CR₉R₁₀)mCO; R₅ = H; R₆ = H, alkyl, HOCH₂, HSCH₂, (un)substituted benzyl; R₅R₆ = (CH₂)₃; R₇, R₈ = CO₂H, alkoxy, carbonyl, (un)substituted CONH₂; R₉R₁₀ = H, alkyl, alkenyl, etc.; R₁₁ = H, alkyl, alkoxy, Ph, cholesteryl, etc.; X = O, S, CH₂, etc.; m = 0-90; n = 0, 1] are prep'd. as drugs for enhancing host resistance against opportunistic infections in **AIDS** patients. 2-Acetamido-1,5-anhydro-4,6-O-benzylidene-2-deoxy-D-glucitol was reacted with L-2-chloropropionic acid in NaH-contg. dioxane to give 2-acetamido-1,5-anhydro-4,6-O-benzylidene-3-O-(D-1-carboxylethyl)-2-deoxy-D-glucitol. This was treated at -15.degree. with DMF, N-methylmorpholine, isobutyl chloroformate, and L-alanyl-D-isoglutamine benzyl ester-HCl to give 2-acetamido-1,5-anhydro-4,6-O-benzylidene-2-deoxy-3-O-(D-2-propionyl-L-alanyl-D-isoglutamine benzyl ester)-D-glucitol, which upon hydrogenolysis over Pd in HOAc gave 2-acetamido-1,5-anhydro-2-deoxy-3-O-(D-2-propionyl-L-alanyl-D-isoglutamine)-D-glucitol. I, administered s.c. at 100-300 mg/kg/day over 5 consecutive days, increased the prodn. of antibodies against bovine serum albumin in mice (no specific examples).

IT **81638-45-1P**